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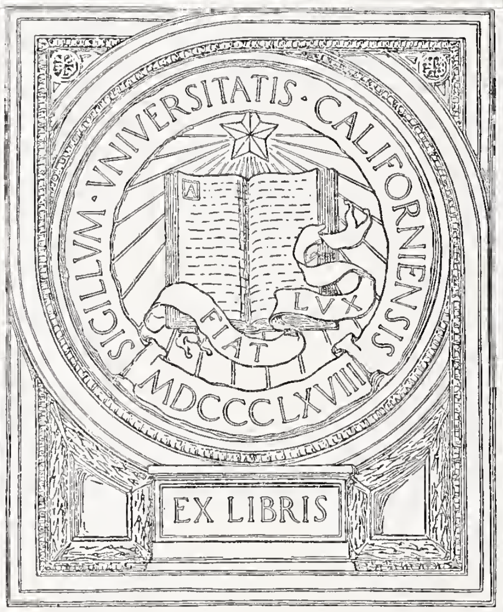

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Connecticut Medicine

Connecticut State Medical Journal

Volume 28 / January 1964 / Number 1

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LAENNEC AND THE STETHOSCOPE (see page 1)

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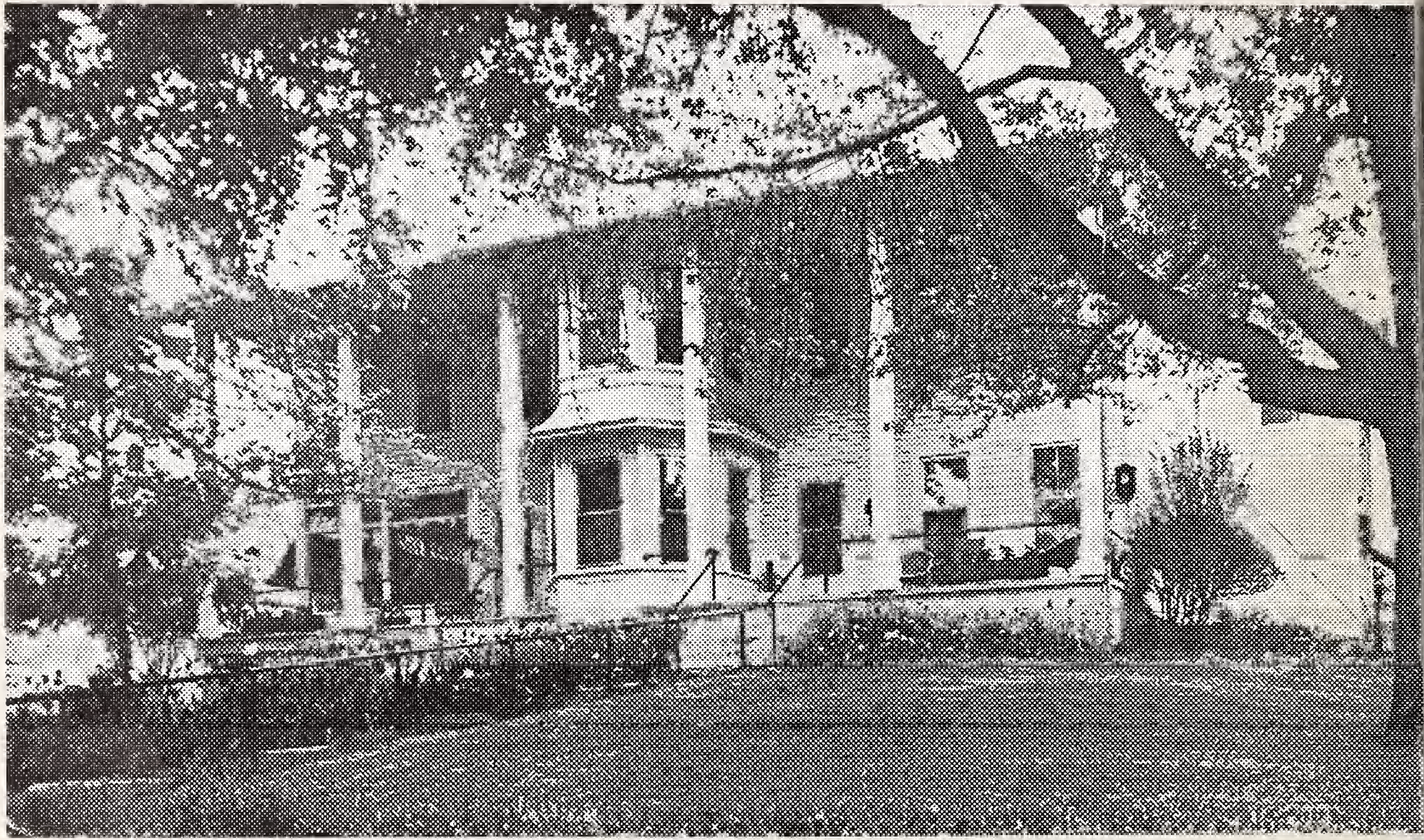

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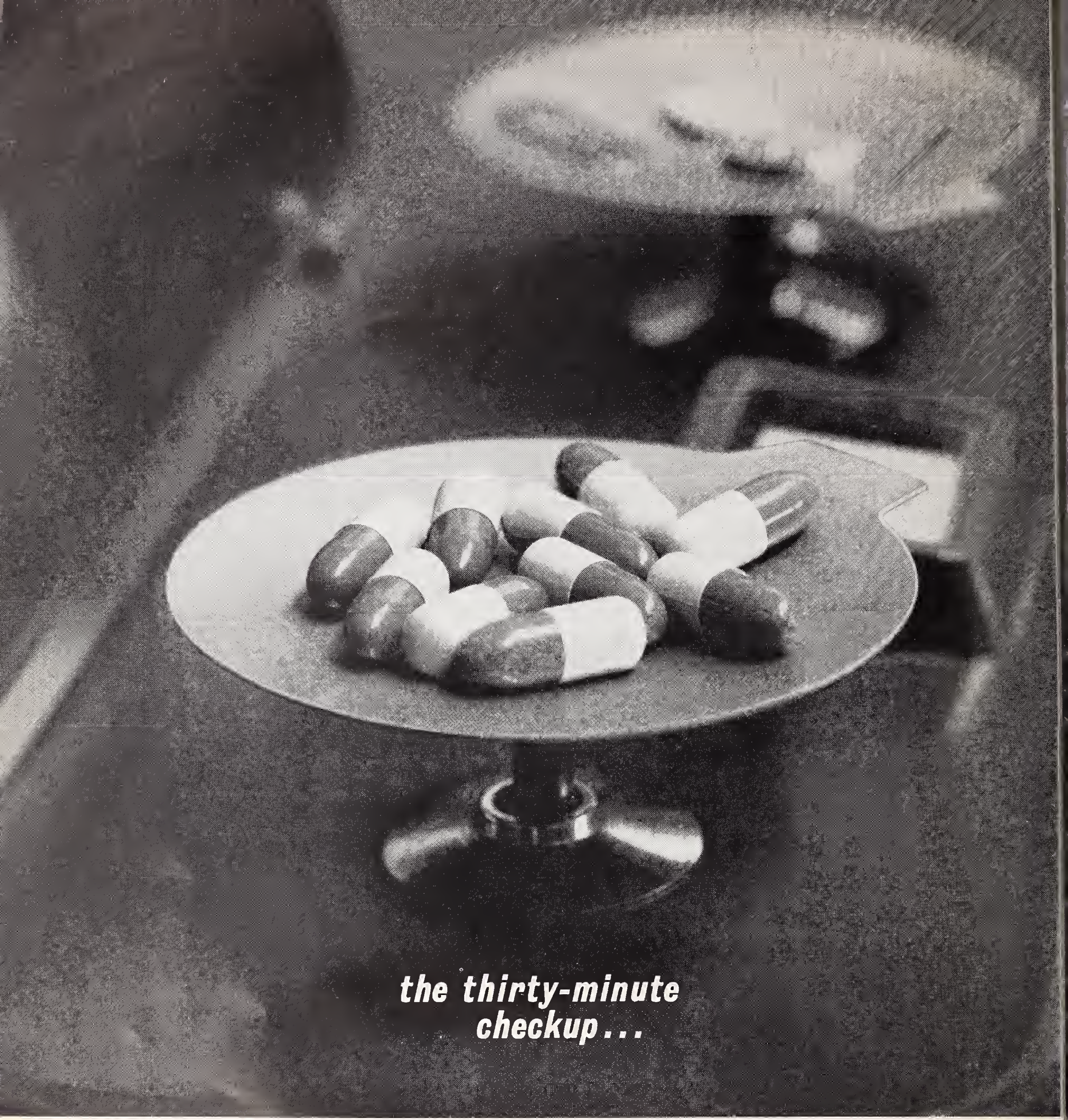

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Connecticut Medicine

editorials

Science Tools:
4. The Platinum Electrode

Clark and Bergeron[1] introduced the platinum electrode for use in cardiovascular diagnosis in 1959. It is based on the fact that a platinum black electrode produces a very sizeable potential with respect to a reference electrode when exposed to blood containing hydrogen. Potentials up to 300 M.V. are observed and thus are relatively simple to measure and record even in the presence of potentials generated by the heart which are greatly lower. Although the potentials developed by the platinum black-tipped catheter are not strictly quantitative, the difference in timing, the rate of response, and the final potentials developed are so great that little difficulty is encountered in distinguishing the presence of hydrogen gas. One inspiration of 100 per cent hydrogen is enough for the hydrogen gas to cross the pulmonary membrane, dissolve in the blood and appear immediately in high concentration in the left heart, and later in lower concentration in the right heart.

This hydrogen sensing platinum black tipped catheter is uniquely sensitive in detecting right to left shunts. By moving the electrode tipped catheter from one location to another, with an inspiration of hydrogen at each location it is possible to detect left to right shunts, that are located high or low with openings that are large or small. Clark and Bergeron have gone further and designed a multiple electrode catheter whereby hydrogen potential measurements can be made simultaneously at various points and where blood samples and pressure measurements can be taken at the same time.

Vogel *et al*[2] have used this method in over 200 catheterizations many of which have been in infants. Some in whom faint diastolic murmurs were present but who showed on catheterization identical pressures and saturations in the right heart who by positive hydrogen curves nevertheless showed left to right shunts. They report other instances in which no evidence of shunt was found by O_2 saturation data, but small left to right shunts at the ventricular level were readily demonstrated by the hydrogen platinum electrode.

As experience with this powerful tool develops, additional uses of the regular single electrode catheter have become increasingly apparent. Many usual procedures may not be sufficient, as in infants with large interventricular septal defects with a possible associated patent ductus. Passing catheters may not bring the tip to the right spot. Withdrawing of blood for indocyanine curves through a small catheter is difficult and angio-cardiography is not without risks. The hydrogen platinum electrode overcomes these difficulties.

Ascorbic acid is also useful in localizing right to left shunts by a small platinum electrode attached to a fine wire insulated with teflon. It is of use in all age groups and can be introduced into an artery if necessary. It can be passed through a transseptal needle into the left heart for the purpose of detecting mitral insufficiency. If insufficiency exists, then the ascorbic acid injected into the left ventricle via a retrograde catheter is detected almost immediately by the left atrial electrode.

THE COVER

LAENNEC AND THE STETHOSCOPE

THEOPHILE LAENNEC (1781-1826), young French physician, while at Necker Hospital, Paris, in 1816, devised foot-long hollow wooden cylinders for listening to sounds in patients' chests. These he called "stethoscopes." Comparing opinions formed during stethoscopic examinations with later findings at autopsy, Laennec learned to accurately diagnose many pathologic heart and lung conditions. His instrument and his published reports on its use were among the greater contributions to nineteenth-century medicine, helping physicians to understand pulmonary diseases—especially tuberculosis, the malady that ended Laennec's own short life.

Bergeron *et al* placed this teflon insulated wire in the pulmonary artery at the time of operation after repair of septal defects for the dual purpose of evaluating whether the defect is closed postoperatively and also for use as a cardiac pace-maker. Watson has recently emphasized the importance of intracardiac electrocardiograms especially in infants. With the platinum electrode one can readily combine the advantages of the hydrogen, and ascorbic acid techniques with intracardiac electrocardiography.[3]

Clearly the usefulness of the platinum electrode in cardiovascular diagnosis is just beginning to be realized. Because of its extreme sensitivity it is bound to make diagnosis more precise. We may expect continual appearance of new applications of this powerful tool.

L.H.N.

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Improper Positioning During Surgery

There have been limited studies on the effect of various positions of the body on certain physiological functions, but quantitative studies regarding the effects of surgical positions on the cardiovascular, respiratory and nervous systems were not available until Eggers *et al*[1] undertook a series of studies on the cardiovascular system changes that are associated with the various positions that are utilized in the operating room. If we knew such effects, it would help to avoid improper positioning. Many positions are used to obtain better surgical exposure, or of allowing more convenience for the surgeon and his team of assistants. But if the consequences of intolerable positioning can be neurovascular injuries, cerebral edema, or locallized vascular stasis, both the surgeon and the anesthesiologist should know about it.

In the anesthetized state when a patient is placed in an unnatural position, he is not aware of it, nor is he able to solicit aid in avoiding unnecessary trauma or stress superimposed upon this unnatural condition. The anesthesiologist is alerted at times to the existence of an intolerable position by such physiologic reactions as hypotension, tachypnea, muscular spasm, diaphragmatic jerking and occasionally by cardiovascular collapse. Even then, the anesthesiologist may not be able to differentiate between the effect of positioning, from other results of the operative procedure itself. Many times whatever warning signs arise from intolerable positioning are either unheeded or are superficially corrected or rather disguised by vasopressors, vagolytic agents and muscle relaxants.

Eggers *et al* studied ten adult male subjects with no demonstrable cardiovascular or other diseases. They were initially evaluated in the supine position in the fasting state and without premedication for pulse rate, arterial pressure, cardiac output, systemic vascular resistance and electrocardiogram. All values were found to be in the normal range. The subjects were then placed in various awkward positions and when they became uncomfortable, studies were repeated. Finally, the subjects were anesthetized and the above observations were repeated in the supine and certain uncomfortable positions. The anesthetic used was intravenous thiopental and 1.5 per cent halothane and oxygen. After ten minutes, 40 mg. succinyl choline was given intravenously, the larynx was exposed and sprayed with 6 per cent cocaine and a cuffed endotracheal tube inserted.

In the awake state the subjects maintained identical mean arterial pressures in spite of awkward positions. In the anesthetized state the mean arterial pressure was considerably lower in the right lateral, right lateral jack-knife and prone positions, when compared with the supine anesthetized subjects. The average systemic vascular resistance was found to have been profoundly altered by the patients positioning in the anesthetized state in all positions except the left lateral.

The mean arterial pressure dropped 20.7 mm. Hg. and the average difference in systemic vascular resistance decreased significantly. Ordinarily, the systolic arterial pressure is affected by cardiac output, blood volume peripheral vascular resistance, elasticity of vessels and blood viscosity. Only the peripheral vascular resistance declined markedly to reduce the arterial pressure while cardiac output, blood volume and viscosity remained constant. Since there was no reduced cardiac output, there could be no reduced venous return.

The hypotension caused by a decrease in systemic vascular resistance can be caused by the anesthetic which Eggers *et al* chose for their study. Apparently they chose halothane because of its frequent and common usage, the absence of explosion hazard, and the relatively few and mild postanesthetic sequelae for the volunteer subject.

It is clear from the study that surgical positions alone have an adverse effect upon the cardiovascular

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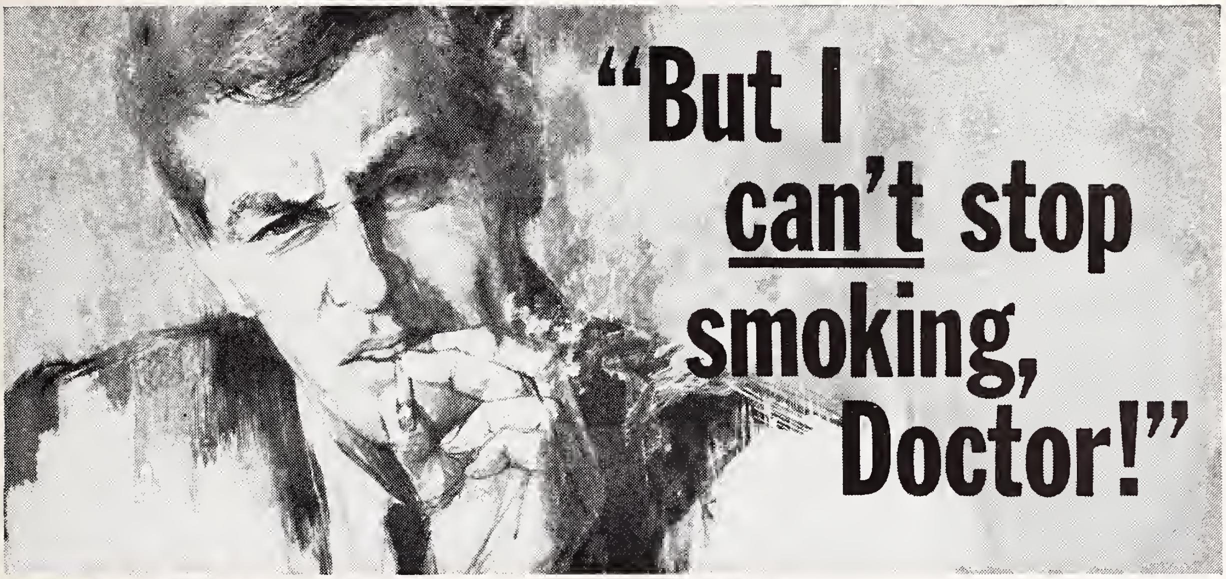

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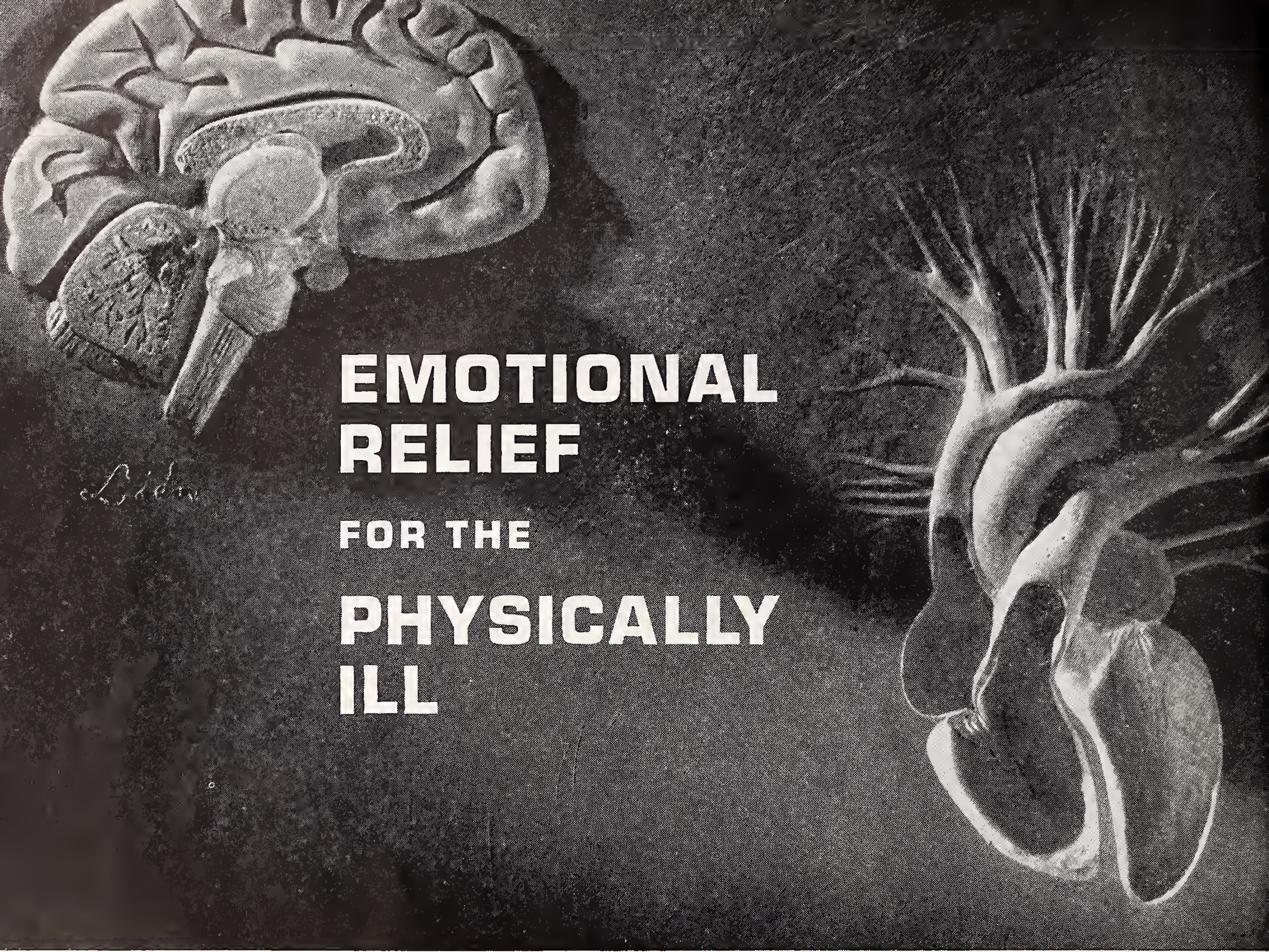

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system even in healthy subjects when anesthetized. Without doubt such effects may be predicted to become more profound in the ill and debilitated. As more data is accumulated, certain positions may be found to be more deleterious than others. Such positions can either be avoided or better positions substituted when compatible with the contemplated surgical procedure. By emphasizing to all surgeons and anesthetists the rather profound effects that improper positioning can have, Eggers has contributed towards better patient care during surgery.

L.H.N.

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Physiology of Obesity

What is it that makes the obesity problem so baffling. No one denies that it is due to overeating, for it exists in every society, but is rarely found in that part of the world that lives on a bare subsistence level of food supply. Nevertheless, even in affluent societies, only certain individuals will become overweight and of these some will find weight reduction relatively easy, but large numbers will find it extremely difficult. Of this latter group, many will lose weight very slowly and with great difficulty when they embark on simple calorie restriction, only soon to relapse and recover their weight.[1] Some will not even lose weight for a long time after beginning calorie restriction, an extremely baffling and discouraging experience.

The phenomenon of a patient subsisting for a prolonged period on a severe calorie restriction and still manifest no weight loss, is a familiar experience to every physician who has studied obese subjects. It appears to be a paradox of thermodynamics and must have some explanation. One can propose the hypothesis that as the body loses fat, it at the same time retains water, thereby avoiding weight loss. There is a physiological explanation for this which is somewhat as follows: 100 grams of fatty acids will yield as a byproduct 112 grams of metabolic water. If not excreted promptly, the metabolic water can completely cancel the loss of body weight that would otherwise occur from the oxidation of storage fat. But why is the water retained instead of being excreted? The water retention seems to be due both to a reduced glomerular filtration rate and also an elevated titre of antidiuretic hormone with a resulting markedly reduced renal clearance of water.[2] Accordingly, when a calorie restriction is imposed, there is a powerful antidiuretic effect and salt is retained even to the point in which pretibial edema may become noticeable. This diminution of water excretion by the kidney is most pronounced in the standing position, when glomerular filtration rate declines, so that almost complete cessation of urine formation can be observed in some patients.

A knowledge of the reasons why some people will overeat and become obese would require a consideration of psychologic factors of which there are many, including anxiety and depression. Nevertheless once a patient becomes obese, in order to understand the rational approach to their treatment, it is necessary to learn whether the problem is a simple matter of calorie restriction or whether there exist biochemical and physiological anomalies in the obese subject as distinct from the non-obese one. One idea is that proposed by Cohn and Joseph[3, 4] that there occurs a real increase in the efficiency of food utilization when food is eaten in larger amounts at frequent intervals. With this goes a 25 fold increase in lipogenesis apparently resulting from an increase in the synthesis of enzymes in liver and adipose tissue that assist in lipogenesis.

Gordon, Goldberg and Chasy point out also[5] that one or two large meals eaten daily also tends to promote storage of fat. They point to the eating habits of the vast majority of obese human subjects describe spontaneously their own efforts at weight control through dietary privation most of the day, with the food intake concentrated at one period most often in the evening. The "night eating" syndrome is an exaggerated form of this same pattern. Furthermore, these authors point to a close relationship between the metabolism of carbohydrate and the synthesis of fat. In fact, the storage of fat and production and maintenance of obesity cannot take place unless glucose is being metabolized. However, glucose cannot be used by most tissues without the presence of insulin. It follows that obesity is impossible unless there is an adequate supply of insulin and an abundant intake of carbohydrate foods.

This combination exerts a powerful influence in directing the stream of glucose metabolism into lipogenesis and this in turn leads to the further synthesis of enzymes in liver and adipose tissue that further promote lipogenesis—a sort of a vicious circle to maintain obesity. If insulin is so important in lipogenesis, it is obvious that obese individuals are using excessive amounts of insulin constantly and we have here a physiologic explanation for the exhaustion of the pancreas and the frequency of diabetes among the obese patients.

Another question that Gordon *et al* posed was whether there are other metabolic abnormalities present in the obese as distinct from the non-obese subjects. In an exhaustive study of a large number of patients, they detail twenty-six different aberrations of metabolism, many occurring in the same individual, varying from hypometabolism and subnormal PBI to other hormonal disturbances involving carbohydrate and lipid metabolism, pituitary, adrenal and renal responses to the challenges of increased food intake.

With such a maze of metabolic aberrations, how does one arrive at a rational therapeutic regimen with the specific intent of correcting if possible, as many abnormalities as possible. As far as hypometabolism is concerned, Gorden *et al* suggest it be managed with triiodothyronine in increasing doses until effects are produced or toxicity appears. This special type of thyroid hormone, in contrast with thyroxin or dessicated thyroid, increases directly and promptly the oxidation of glucose in those patients that had previously manifested a depressed rate of oxidation. Because of the stimulating effect of glucose on lipogenesis, the carbohydrates are kept low. Triiodothyronine, which at first was used only in hypometabolic patients, was gradually extended by Gordon to all patients, unless they suffered from coronary artery disease. The rationale appeared to be the need of diverting the metabolic machine from lipogenesis to complete oxidation of glucose to CO_2 and water.

The problem still remained as to how the metabolic pattern geared to lipogenesis can be broken. Here again animal experiments have pointed the way. Hollifield and Parson[6] showed that this metabolic pattern could be most easily broken by imposing a forty-eight hour fast on the animals. After this period, continuous availability of food to the rats led to a restoration of a normal eating pattern, atrophy of the previously hypertrophied enzyme systems, and a return to normal low levels of lipogenesis. There thus appeared to be a justifiable reason to believe that in patients also a brief fasting period might change the tendency to lipogenesis back towards a normal pattern of glucose oxidation to CO_2 and water. This in fact was the encouraging and surprising experience of Gordon in his patients. During the forty-eight hour fast, no patient complained of hunger though there was some withdrawal unhappiness for a short time.

The results from the use of carbohydrate restriction, triiodothyronine and a 1320 calorie diet after a period of forty-eight hours of fast were uniformly successful. There developed a spontaneous evolution of new and beneficial dietary habits in a great many patients who commented with great surprise about the apparent loss of old compulsions to eat, and about the modifications of their cravings for certain high carbohydrate foods. One thing seems clear from this important study that severe calorie restriction is not the correct way to manage obesity, since it provides no opportunity for readjustment and re-education of the patients dietary habits.

It is still not possible to know which are the causes and which are the effects of obesity. What about the baffling question of the relative importance of genetic factors as compared to the self-evident adaptive or environmental factors. Do the striking metabolic deviations from the normal in most of the patients mean that obesity represents a separate clinical entity or is metabolic obesity merely a stage of the obese state and related to the duration rather than the degree of obesity? Only increased experience can provide the perspective necessary for a final correct interpretation.

L.H.N.

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The Doctor As Therapist

It is possible to gain an insight into principles that should govern physician patient relationship from a study of an isolated segment of medical practice such as how accidental injuries are managed, just as it was possible for Freud to lay down concepts in normal human psychodynamics from a study of the abnormal—the neuroses. Behan and Hirschfeld have done just this in a study of 300 industrial accidents. From an analysis of the behavior of injured patients, they have gained an insight into the problem of physician patient rapport which is central in the whole practice of medicine. What the elements of this rapport are, how to avoid rejection of the doctors ministrations by the patient and the pitfalls in the doctors attitudes that can disrupt rapport are brought out in a true preceptive manner by these authors. They

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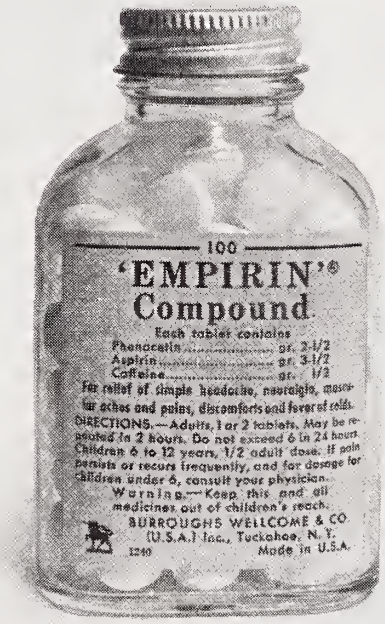
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show clearly how patients become hostile to their would be therapists and how this produces a remarkable and often non-therapeutic reaction in the physician.

Previously in these pages it was made clear that what patients want in their physician is competence and that only 16 per cent of patients worry too much about the physician's personal relationship with them. This however, is not the whole story. What about those patients in whom symptoms represent a solution to their life's problems. Patients to whom an accident and continuing symptoms are an emotional boon and a self-destructive psychological process. Or those patients in whom a simple occurrence like a burn or a viral gastroenteritis leads to mounting fear or panic. The impression of indecision which the patient may gain from the doctor's attitude, does nothing but to enhance the fear. Here competence alone comes into question. In such circumstances patients might continue unproductive treatment and the physician become enmeshed in ambivalent, insecure or even hostile responses that disrupt rapport and make the therapeutic relationship ineffective. In short, the physician's attitudes are really central and can become the major determinants of the outcome of therapy.

This is in contrast of course, to purely surgical problems or of many bacteria related diseases where in the techniques of treatment consists primarily of mechanical procedures or of the judicious use of medications. It is in those situations when the physician deals with medical problems that are generated or continued by psychic or social problems in which the chief therapeutic agent must continue to be the physician himself. If he recognizes these forces and takes time to understand them, then he will be a "human antidote" and his constructive attitudes can yield much benefit to the patient as well as great satisfaction to himself. Where psychosocial factors are involved, it has repeatedly been demonstrated that even the first instant of contact with the patient can profoundly influence the outcome of treatment.[2]

Behan and Hirschfeld have recognized that three main results flow from disturbances in the doctors reaction to such patients, disturbances in rapport, overcompensation and retaliation. They point out that the therapeutic effect of the doctor himself can be easily understood if one considers the phenomenon of mental images which determine relationships between people. If these mental pictures are such that the patient feels safe, unguarded, and in the presence of a competent ally, then therapy has begun. The patient needs to feel he is in the hands of a competent doctor. What physician has not heard a patient say "now that you are here I feel better already." Contrariwise, in the absense of proper mental images, indifference to the patients suffering, or his problems, indecision or hostility, on the part of a physician, then the entire rapport is lost. This is especially so when a patient needs to continue his suffering as an expression of unconscious guilt. He may set out to fool the doctor with aggression, silence or other means. In this way, the doctor is doubly attacked. There is an effront to the good opinion of himself and the patient and doctor are really at loggerheads. At best, the doctor feels confusion and uncertainty. This is known to be especially true in medical students since Parker[3] has shown that the more uncertain the status of the student, the more hostile and cynical become his attitudes towards patients. This was equally true of the graduate physician who is shaken by the patients mistrust. He may prescribe much pointless treatments, he may oblige a patient who is seeking punishment because of unconscious guilt by hostility and counter angry reaction, though he is usually unaware of the real nature of his actions.

If a physician is being systematically provoked towards punishment of the patient and if he also feels confused and uncertain, then he is angry and in a grossly untenable position and the therapeutic process is destroyed. A hostile patient is faced by a hostile doctor and no chance of rapport can exist. From the first moment we enter a medical school we are taught that it is unprofessional to express hostility towards a patient. We cannot show rage and hostility. But we are human and suppress these feelings. We let our diligence compensate for our unacceptable feelings. Wo do an especially careful examination, we miss nothing. Perhaps an extra X-ray, extra medication, extra myelogram, extra laboratory procedure, a little extra traction or more physiotherapy is undertaken. The doctor is now overcompensating.

The difficulty of course, is caused by the concept that a physician is not morally entitled to anger and if he exhibits it or feels it, he is ashamed, he wants to hide the thoughts. Thus both the anger and its results are forced to disappear from consciousness. But they are not gone, and they play an important role in his attitude. There is little doubt that attitudinal problems of the therapist determine whether good or bad results will be achieved. This is as true in non psychiatry as in psychiatry.[4] Other reports have recorded similar findings. Stoller[5] found from a study of senior medical students that their attitudes towards patients whose somatic symptoms were of emotional origin were very similar to our own vision of the practicing physician. The students saw such people as aggressively demanding of all with whom they came in contact. They did not, as many physicians do not, realize the need on the part of such patients for punishment to assuage their unconscious guilt. Neither were they aware of their own repression of hostility. How similar to the mental images mentioned above.

What can be the remedy to such a non therapeutic relationship? Behan and Hirschfeld suggest the following. First is not to be afraid to recognize that a condition should be considered psychogenic, unless symptoms can be clearly explained by a normal response to an anatomical or pathological defect. In the absence of pathology a chronic illness should be considered psychogenic unless proven otherwise. Many important authors now support this position. This of course, requires a change in our medical thinking, because physicians tend to reserve a psychiatric diagnosis until all others are excluded. In part this attitude is related to a belief that psychiatry is a discipline of vagueness and inexactitude, an area of the indefinite. Because of these beliefs the patient's history is rarely searched for details relating to why some patients continue to hold on to their symptoms in order to avoid facing problems of life.

The authors have also noted that physicians do not make a succinct statement of the patient's problem and tend to hide behind labels such as "excitable foreigner, emotionally unstable, a complainer, the type who would take advantage of compensation."

The truth of course, is that criteria for diagnosis of neurosis, psychosis and personality disorders are now clearly defined and can be learned by any clinician. When they are adequately diagnosed, they still leave room for a sharp diagnosis of physical disorders which often occur and may be constantly added. For example, a man can have a lumbar sprain. Still if he does not recover for say a period of three weeks after the anatomical change should have resolved, this does not invalidate the effect of injury, but it does tend to prove that now the patient has begun to bring his back symptoms into the service of his psychosocial, economic and legal conflicts. In short, symptoms can result from anatomical change, but their persistence or aggravation may mean that the same symptom now represent emotional causes. If the physician can sharpen his diagnosis at the moment when symptoms should disappear if they are based solely on organic pathology, then there is considerable possibility of improvement.

The best therapeutic instrument turns out to be not the psychiatrist but the treating physician whose knowledge of the whole person enables him to use both psychic as well as somatic tools. But such a doctor would need some psychiatric background. He should be able to perform a proper, careful and extensive physical examination so that he can reassure his patient and finally be able to probe into the patient's motivation. He should have not only medical expertness, but a personality capable of assuming both responsibility and leadership using specialist services when necessary, but co-ordinating, tempering, and supervising. He will regulate everything that happens to the patient. He will be the captain of the team. This is upgrading the role of the family doctor but it will be an important and beneficial change in his present role.

The material contained in Behan and Hirschfeld's paper suggests a necessary characteristic of the physician. He may be exposed to resistance and hostility on the part of the patient he is treating. He will therefore, need to be able to deal with his own moralistic tendencies to repress his own hostility. Handling this effectively will make it possible to eliminate the destructive effects of unconscious and therefore, uncontrolled hostility in both the patient and himself. This of course, implies that the physician be well versed in the techniques of psychiatry.

How does an internist become acquainted with this discipline? There is no such thing as "common sense psychiatry." Behan and Hirschfeld suggest the seminar method which are held weekly and in which cases are reported by the trainees and discussed with them by a psychiatrist. This methodology allows for an interchange of information which will also benefit the psychiatrist. According to Balint[6] it can change for the better the relationship between doctor and patient.

The result of such an orientation would be a change in the history taking procedures. It would establish the correct contact between physician and his patient technically called "Rapport."

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A Model For The Study Of Auto-Immune Mechanisms

We are on the threshold of successful organ transplantation and need to know more about tolerance and intolerance of foreign grafts. Then there is a host of diseases associated with the autoimmune process such as disseminated lupus, periarteritis nodosa, rheumatoid arthritis, hemolytic anemia and autoimmune nephritis, myasthenia gravis, antibody against thyroglobulin in pernicious anemia and many others yet unknown. Furthermore, it has been well recognized that in one individual, there may appear more than one manifestation of autoimmune disease and that these are now known to be frequently familial. To experiment on humans is difficult. What has been lacking up to the present time is an experimental model which would provide an opportunity to investigate the multitude of problems in relation to auto-immune disease. Without an experiment model, only vague and hesitant steps have been taken such as thymus gland removal in myasthenia gravis.

Up to the present we know that the thymus plays an important role in immunologic reactivity.[1] With this organ the body gains the ability to defend itself against bacterial infection and against invasion of foreign substances incompatible with the body's well being. But the mystery deepens when the body develops antibodies against its own tissue, setting up diseases against which we have little recourse. An ideal experimental model has been produced by Bielschowsky, Helyer and Howie[2] in the form of a special strain of mouse NZB all of whom develop serological and pathological evidence of autoimmune disease during adult life. These mice exhibit two outstanding lesions. One is the development of germinal centers together with a variety of secondary changes in the thymus around the time when the Coombs test becomes positive. The second is a severe terminal nephritis especially characteristic of females. The major lesions are in the basement membranes of the capillary loops of the glomeruli with subsequent involvement of the tubules as well.

Young NZB mice are invariably Coombs negative up to 100 days of age.[3] Eventually a permanently positive reaction develops with agglutination, shown also with 1:50 dilution of Coombs serum. In old mice their red cells often agglutinate spontaneously in saline. On two occasions a Coombs test, positive for months reverted to negative in old mice and in both, spleen architecture had been replaced by leukemic tissue. The Coombs reaction appears to be initiated by an internal "trigger" whose time of functioning is modified by sex. Once initiated the process persists throughout life. It would seem as if a single type of antibody with widely varying degrees of "avidity" and completeness was involved.

The central feature of the studies by Holmes and Burnett[3] is the demonstration that in the NZB mice the discoverers have given us a model system which appears likely to present real analogies to a wide range of autoimmune conditions in man. The two features which have become progressively clearer about human autoimmune disease are: first, the genetic (familial) component to the etiology; and second with increasing study of individual patients, it is the rule to observe more than one form of autoimmune conditions. Antibody against thyroglobulin is unduly common in association with pernicious anemia. Rheumatoid arthritis patients show a relatively high proportion with antinuclear factor (ANF) in the serum. "It seems that there is a basic genetic characteristic or more likely a group of genes or gene combinations with relatively low penetrance which predispose to the eventual emergence of manifest autoimmune disease."[3]

Why is it that the thymus and perhaps also the spleen and lymph nodes are functioning abnormally and together are launching a massive attack on a number of essential organs both by cellular elements such as lymphoid and plasma cells and by autoimmune antibodies. Is it all genetic? Are there other possible factors in combination with the genetic apparatus over which we might gain control. Accordingly perhaps a very important problem which work on the NZB mice may help to solve is *what* in a genetically predisposed individual determines the nature and the timing of autoimmune manifestations which emerge to the clinical level. At present there is much to suggest but as yet, little to prove, that the usual onset of an autoimmune disease like disseminated lupus results from some trigger stimulus which sets in motion "a process of basically autocatalytic self perpetuating character." What are such stimulis and how can we avoid them?

Little is on record about histological findings in thymuses for other autoimmune conditions besides myasthenia gravis. Most autopsy material is very unsuitable owing to involution by age and illness. It seems particularly desirable that a new approach be made to the thymic histology in autoimmune disease, particularly in children and young adults, in order to establish the picture of a normal thymus at autopsy and how subacute or chronic illness or corticosteroid therapy alters the normal picture. We also urgently need knowledge on whether thymuses from autopsies of cases of different autoimmune conditions show any significant differences from the normal. Observations on NZB mouse strain should point the way to provide an answer to such questions.

There are many other problems that studies on our experimental model might illuminate. Would thymectomy be of value in disseminated lupus in young women as it appears to be in the corresponding group of myasthenia gravis cases? If this procedure were undertaken, it would provide much more satisfactory histologic material. It should soon emerge whether and how the changes in the thymus are related to the autoimmune process. Why is it that all manifestations of hemolytic disease begin earlier and are more intense in males than in females. Why do thymic lesions appear much earlier in females and why is there a greater incidence of severe glomerulonephritis. What is the explanation for the fact that when male mice are splenectomized between one and three months of age they show diminished effects of hemolytic disease and a sharply increased prevalence of severe nephritis.

It is clear enough that the production of the NZB mouse strain was an outstanding contribution to the field of immunology. This unique biologic model mirrors much that is characteristic of human disease. It should provide an opportunity for the investigation of a multitude of important problems in relation to autoimmune disease.

L.H.N.

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Avoiding Pitfalls In External Cardiac Compression In Infants And Young Children

It is now recognized that the treatment of cardiac arrest with external cardiac compression in infants and small children terminally, is associated with various injuries to the liver varying from minor trauma to occasional rupture which in itself could cause death. How these are caused and how they should be prevented is the subject of an excellent study by Thaler and Scobie.[1] After preliminary experiments on dogs they turned their studies to fresh human cadavers within three hours of death, subjects that had not sustained prior injury during life. In experiments in fifteen cadavers, liver rupture was found to be due to simultaneous compression of the chest and abdomen, thus limiting free movement of the liver. When the pressure was applied to the chest alone, no rupture of the liver was produced, even if excessive pressures were used. However, superficial tears of the capsule over the diaphragmatic surface of the liver resulted from sudden sharp pressures applied with tips of the fingers to the xiphoid, thereby tearing the ligamentous moorings of the diaphragm and Glissons capsule.

No rupture of the liver or injury to other abdominal organs resulted from pressure to the abdomen alone. But when simultaneous pressure was applied both to the chest and the abdomen, this resulted in liver rupture. Apparently, when downward movement of the liver into the abdomen is prevented by chest cavity compression, then the congested liver parenchyma burst through the tense capsule usually between the right and left lobes. Superficial lacerations and subcapsular hematomas can also be produced by such inappropriate compressions.

Their findings naturally suggested that moving the site of compression away from the abdomen and xiphoid end of the sternum would result in a safer technique. Whether effective circulatory pressures could be achieved in this manner, of course, depended on the anatomic characteristics of the infantile thoracic cage and its relation to the heart. Radiographic studies on twenty cadavers demonstrated that the heart in young cadavers occupy a high position within the young thorax and that the neutral surface underlies the middle sternum in infants and young children, whereas the lower end of the sternum is actually superimposed on the liver. During growth, the heart gradually descends so that in the adult its position comes to lie behind the xiphisternum. Accordingly, external pressure applied to the middle of the sternum in infants and young children compresses the ventricles, whereas pressure over the xiphoid end directly affects the liver. For this reason it required less pressure in the midsternum to achieve 100 mm. Hg. pressure, than when the pressure was applied lower in the chest.

The small size and great flexibility of the chest combined with relatively large surface presented by the heart in an infant, make external application of pressures easy and effective. The chest cage is barrell shaped, there is a large space between the sternum and the spine and a high lying voluminous heart. At the same time because a part of the sternum overlies the liver, it is easy by using the heel of the hand to compress not only the heart but the liver as well, and it is this maneuver that must be avoided to prevent liver trauma. Apparently

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the simple factor of excessive pressure, provided it is applied to the chest, will not by itself produce hepatic trauma.

The teaching of external cardiac compression suggested by the authors for infants and children consists of compression of the midsternum with superimposed thumbs while the fingers are linked behind the patient for additional support. The ribs are left free to expand during artificial respiration, which can be carried out in a mouth to mouth position every five seconds by the same operator. If the electrocardiogram shows ventricular fibrillation then of course, defibrillation is indicated. When the electrocardiographic pattern becomes normal, the external massage is continued at the rate of one per second until an effective circulatory pressure can be maintained by the heart without further assistance.

The study was necessary, since following the publication by Kouwenhoven, Jude and Knickerbocker[2] the procedure has become common practice. It was discovered that cardiac arrest occurs comparatively often in infancy. A recent ten year survey[3] showed nearly a three fold incidence of arrests in infants under one year of age as compared to all other groups. Because there is greater tolerance to anoxia in premature and term newborn infants, at least theoretically, there should be a higher percentage of successful resuscitation in this group. Successful resuscitation is also favored by the small size and greater flexibility of the chest and relatively large surface presented by the heart in an infant to make external application of pressure easy and effective.

The work of Thaler and Scobie was carried out in the best tradition of experimental science. Observation of liver trauma in attempts at cardiac resuscitation in infants, stimulated anatomical studies, which revealed the right and wrong places for external compression. Further studies on hemodynamics, clarified the amount of pressure necessary to sustain a good blood pressure. These observations led to the establishment of a procedure for external cardiac resuscitation in infants and young children which is both safe and effective.

L.H.N.

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Antivert And Meniere's Syndrome

Antivert (Roerig), a combination of 12.5 mg. of meclizine and 50 mg. of nicotinic acid per tablet, is claimed to provide quick relief of "Vertigo, Tinnitus, Meniere's Syndrome, Labyrinthine Disorders [and] Allied Disorders." To support the claims, advertisements for the drug refer to an uncontrolled study of J. C. Scal (Eye Ear Nose Throat Monthly, 38: 738, 1959) showing improvement in 46 of 50 patients with "Meniere's syndrome." This is one of numerous uncontrolled studies which assert the benefit of one or another drug in relieving vertigo, but ignore the tendency of this and related symptoms to improve spontaneously and unpredictably. Only in vertigo associated with motion sickness have adequately controlled trials been carried out.

Vertigo frequently involves a considerable emotional element and often presents difficult problems of diagnosis and treatment. If such causes as intracranial neoplasm and the toxic effects of such drugs as streptomycin (Medical Letter, 1:29, 1959) can be excluded, recourse to symptomatic remedies (or to placebos) is justified. Meclizine, one of the ingredients of Antivert, or some other antihistamine drug may be worth trying (antihistamines are often effective in motion sickness [Medical Letter, 3: 49, 1961]). Scopolamine and sedative drugs are also effective in some patients, as are diuretics or a low salt diet.

Nicotinic Acid—Nicotinic acid, the other component of Antivert, is a specific in the treatment of pellagra, and large doses have been used to reduce the cholesterol level of the blood. While such doses frequently produce flushing of the skin and other side effects, the smaller amount present in Antivert is less likely to produce side effects.

Nicotinic acid causes dilatation of the vessels of the skin but not of the arteries of the brain or of the muscles. Nevertheless, it has been claimed to be effective in a large number of miscellaneous and unrelated disorders, including migraine, trigeminal neuralgia, peripheral vascular disease, herpetic eruptions, coronary disease and many others. There is little or no foundation for its use in any of these disorders, or in vertigo. Meclizine (Bonine-Pfizer) is therefore better used by itself than as an ingredient of Antivert.

British medical journals have noted a possible association between the use of meclizine with pyridoxine (Bonadoxin-Roerig) in pregnancy and the development of congenital anomalies (Brit. Med J., 2: 1681, 1962). The evidence for a causative association is unconvincing.

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THE PRESIDENT'S PAGE

Free Medicine?

For some reason American Medicine of the sixties is "up for grabs." Politicians want to control it. Labor wants it for free. The "aged" have been jockeyed into the position of demanding as a right what has never been denied them. On the fringes are the welfare elements, the socio-economic wizards, the "do-gooders," all yapping at the heels of a suddenly bedeviled medical profession whose chief reaction is one of deep puzzlement.

Considered as a specialized profession has American Medicine done badly by its trust to care for the medical needs of our society? Has it been remiss in progressing in an era of rapid progress? Has it neglected to do for the well that which needed doing to keep them well, and to do for the sick what no one can do better? Why the hue and cry over medicine?

Thirty-five years ago there was no such hue and cry. Then those who are now aged were just planning for a future which they alone would be responsible for. In an era far less prosperous but relatively more stable, it was possible to plan ahead. Insurance companies promised retirement to an enjoyable leisure with an insured income of $150.00 a month for those who planned ahead. Whose fault was it that their nest egg shrank to a third of its original value when they became "the aged."

Could it be that the drive for free medicine is motivated by money? We in medicine protest that we have no control over the nation's finances. The responsibility must rest on those who control money. To turn to government control of medicine in order to cheapen medicine is to really cheapen it, but not in the financial sense. Government has never operated anything for less money, whether it ran the railroads or built ships. The common denominator of all government control has been a sky-rocketing rise in cost of operation, a corresponding slide in efficiency, and an increase in taxes to make up the inevitable deficits. To expect that government operation of medicine would be less costly is a delusion. To contemplate the end result of governmental control is horrifying.

We seem to be living in a society whose code of ethics and moral tone has deteriorated to the point where the difference between right and wrong is blurred. Segments of our population who once took pride in self-reliance and the ability to solve their own problems, are no longer shocked at a generation which has been brought up to expect that no matter how badly they fail, a government agency will bail them out. A generation which has been conditioned to look to government for all forms of assistance has even perfected techniques whereby such assistance permits them to live without contributing anything to the society on which they are dependent.

Nations have lived or died because their moral codes, once high, deteriorated. When in the past, great empires fell one could trace their decline in large part to the increased paternalism of their governments and the declining moral codes of their populaces. We have our own modern examples of the disastrous effects of public avarice coupled with government temptations for political gain.

The greatest empire the world has known, has disintegrated before our eyes under the misguided tutelage of socialist governments. By contrast, our defeated enemies have prospered beyond their wildest dreams where the democratic process has permitted them the benefits of private enterprise.

American medicine is great because the American Medical Profession is great. It has perfection as its goal, and if it falls short of perfection it is only because, like everyone else, doctors are human.

There is no such thing as free medicine. There is only the choice of paying for medicine on a free and individual basis, or of paying for it on a controlled governmental basis, and paying, and paying, and paying.

Morris P. Pitock, m.d.

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Alan A. McLean, M.D., New York, Moderator

CHANGING CONCEPTS IN THE MANAGEMENT OF LARYNGEAL CANCER

Tuesday, February 11 - 2:00 P.M.
George A. Sisson, M.D., Syracuse, New York

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Richard A. Overholt, M.D., Boston, Mass.

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Thursday, February 13th - 9:30 A.M.
Joint meeting of Section on Pathology with Section on Radiology

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Thomas P. Almy, M.D., New York, Moderator

PANELISTS: Ray Crampton, M.D., Hempstead
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Body Image And Reaction To Amputations

Ronald R. Kyllonen, M.D.

■ A hospital for crippled children presents many complex problems, some of which have never been enumerated in the medical literature. The author has had the opportunity to participate in the treatment program at the Newington Hospital for Crippled children during the past year, as a part-time psychiatric consultant. The training as a Child Psychiatrist has given an understandably different point of view from the surgical team. The usual practice is to focus primarily on the surgical problem. Unless other problems interfere with the surgical management, no attempt is made to deal with them and frequently they are assumed not to exist. Yet children under-going surgery experience emotional reactions to varying degrees. Usually the reactions are masked so that their meaning and content is rendered obscure. Of particular interest are children who have had a congenital loss of a limb or subsequent amputation due to other causes. The purpose of this paper is to present the need for careful consideration of the individual child's emotional reactions and suggesting steps whereby the surgeon can deal with them.

In the process of maturation, the infant, with his very immature central nervous system, is confronted by a steady series of contacts with the external environment. The result is a constant barrage of external tactile, visual and auditory stimuli from those around him and a steady in-put of proprioceptive and more purely internal cues. As the child's central nervous system matures, these are organized, on a neurophysiological basis into a matrix, which constitutes what can be called the "body-image." On this is based our spatial orientation and self-perception. As Levin[6] has stated, each object one sees excites in the brain a pattern of neurons (engram) specific to that object. In our development, the result is a central image on a neuronal basis of our body and its parts. This "body image" is what we refer to as one's subjective perception of self. We all possess an image of what "we think" we look like. At times we see evidences of distortions, as the adolescent girl with anorexia nervosa, weighing 56 pounds, who has the firm, fixed belief that she is fat. In like fashion, we see people who view genitals as repulsive, breasts as objects of extreme pride, physique and physical coordination items of concern and focus, responding to their "body image."

A necessary and essential factor in the formation of the body image is the qualitative as well as the quantitative sensory experience. This experience may be the way the parents' attitude is transmitted to the child. Truly accepting and loving parents communicate clearly their feelings by the nuances of physical interaction. In the same fashion, parents who have negative feelings transmit them to the child. Disturbances in the integration of body image probably occur in children with physical or neurological defects. Part of the success of the habilitative techniques for cerebral palsied children depends, I believe, on the intensive, close physical contact and sensory in-put that accompanies the therapy.

The habilitative techniques, of necessity, require repeated, intense, close physical contact in which the child is repeatedly and systematically subjected to a steady series of proprioceptive and tactual stimuli. He is jostled, cuddled, stretched, stroked, and moved about in an active intensive fashion. The people he has this contact with are devoted, kind, understanding people, interested in his progress, security and interaction. As a result one can notice steady improvement in social relationships, manner of relating, and expression of affect.

Of particular relevance is the parents' attitude toward the child, his body and its parts. Kolb[4] has stated, "The attitude of the mother and of the father concerning the body of the child leaves its indelible impression on that child as far as his later concept of himself as a person is concerned." In the case of the congenital amputee, the critical factor is the parents' attitude, particularly if the child arrived in the midst of some negative feelings. As Lambert and Sciora[5] have stated, "The child interprets his defect according to what it means to his parents . . e.g., there seemed to be a strong correlation between the parental acceptance and the child's adjustment, not only to his amputation and prosthesis but also to his general adjustment in his daily activities." If the parents are comfortable in their reaction to the defective limb, the child also will learn a comfortable attitude as well. If there

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existed in the mother during the pregnancy strong hostile feelings or preoccupation with folk-lore superstitions, the problem becomes greatly compounded.

We have two different, yet related, circumstances in the congenital amputee and the child encountering amputation later in life, that is, beyond the age of two or three. For the purpose of this discussion, we will consider them separately. Two cases will be presented in each category.

J. P. is a 10½-year-old girl who was born with a congenital amputation of the left forearm. Her birth history was unremarkable, except for the fact that the mother had a course of treatment for lues in 1936. She was referred here at seven months of age in 1952 and has been followed in the Orthetic Clinic since. At age 2½, she was given a below-elbow prosthesis, and in her following visits it was noted that she had an aversion to use of the device. At ages 3½ it was noted that she was still on the bottle, not toilet trained and was not using her prosthesis adequately. She was admitted to the hospital for a period of training. Her success in the hospital did not continue when she returned home, and in March of 1959, the mother was given a brief psychological evaluation in hopes of resolving the problem. In September of 1960, she discontinued all use of her prosthesis. A year later the prospect of a prosthetic hand with some function as well as some cosmetic value was discussed with the mother in hopes of encouraging use. In November of 1961, the prosthetic hand was delivered.

As a clear expression of the mother's lack of acceptance and unrealistic attitude toward the deficiency, arrangements had been made the week preceding delivery of the appliance for J. P. to take piano lessons "now that she has a hand". The unrealistic expectations were shattered when the hand was delivered, and the child dropped the limb and fled with the mother. After all this time, the mother, and consequently the child, was unable to accept the situation. We can predict this girl will continue to have problems, and the future focus of her personality organization probably will center about her deficit.

B. S. is a 34-month-old white male, who was born a congenital below-elbow deformity. At age six months, he was referred to Newington Hospital and was given a passive-mitt type of prosthesis, and by age 2½ was fitted with an activated hook and elbow lock and is doing quite well, despite the fact that the mother has not been completely cooperative with the clinic visits. He appears to be doing well though it is still too early to predict with accuracy the ultimate outcome. The main reason for the success is the mother's attitude. Despite the fact that she is not an ideally cooperative mother, she appears to have accepted the deficit without too much difficulty. The failures of appointments more simply reflect her total personality.

These observations may explain why it has been noted[5] that parents of "acquired" amputees accepted the deficit more easily than parents of "congenital" amputees.

Lambert & Sciora[5] reported that in 182 cases of follow-up contacts, there was good correlation between the total daily wearing time and "using ability". (This has been our experience as well.) However, Lambert & Sciora observe if the more basic psychological needs were not met, hands were no better than hooks as far as use was concerned.

From the standpoint of integration of the prothesis into the body-image, before the pattern is set, it is critical that the child be equipped with a prothesis early in life. It has been the practice to fit lower extremity amputees early so that they could learn to walk as soon as they are sufficiently mature. Even if this fitting is delayed, the advantages of bi-pedal ambulation will quickly outweigh any reluctance to use the device. Aitken has pointed out that before the age of 12 years "there is no social compulsion to walk well; the end is to obtain enough speed and stability to compete with others of his own age."[1] We see, therefore, few problems relevant to the lower extremity, and a greater difficulty, both from a mechanical and a psychological point of view, with upper extremity amputations.

For many reasons, the method of fitting upper extremity amputees at 5, 6 or 7 months of age is ideal. This is about the time that children are using both hands in palmar prehension, which corresponds to their state of physiological readiness. This is also the time when the pattern of hand use is established, and our experience has been to see the children rapidly acquire a sense of possessiveness toward the prosthesis as if it were literally a part of themselves. If the fitting is delayed, they have the opportunity to establish a pattern of use of the stump, which has to be unlearned in order for them to get good use from the prosthesis. When they master this simple device, then they progress to use of a functional terminal device. The chief criterion used to evaluate progress is the child's maturational state of readiness, not age.

This experience is in close agreement with Aitken and Frantz.[2] They approached the problem from the standpoint of developmental maturation and stated, "It is believed the most satisfactory terminal device from birth to 2½ years is a passive type of mitten that offers some cosmetic restoration and yet permits palmar prehension." They did not feel a cosmetic hand was necessary until the "teen years". They also discovered that fitting could be accomplished as early as 5 to 6 months of age, though they believed that proper grasp and release action was not obtained until 24 to 30 months of age.

It has been our experience that even if the hook is not activated by the conventional cable and harness, the child does use the hook to manipulate objects placed in it by parents or himself. He thus had a functional device and an early opportunity to adapt himself to quadrapedal crawling, rather than tri-pedal crawling. This gives him an opportunity to use and develop the associated musculature and we do not see the marked asymmetry seen in children fitted later in life.

Here the child and parents are seen intensively. The appointments are frequent, the entire team is present, and the parents are included in the procedure of the examination. The child demonstrates his use of the prosthesis, the stump is inspected, questions as to use are asked of the child and parents. In the case of child and parents, this encourages them to calmly consider the defect and to facilitate calm acceptance. Many parents cannot easily discuss the defect and early opportunities to talk about it with understanding and supportive staff do help. In addition, a valuable feature of the process is to encourage child and parents to touch and handle the stump in a supportive setting and help them accept the deficit more comfortably. This procedure places the burden on the pediatrician to deal with the problem by discussing it directly, very early, and recommending a planned series of follow-ups with the orthopedist and appliance shop during the first year of life. This will help to stave off the acquisition of negative attitudes of denial before they can take firm hold. These findings are in essential agreement with Kolb,[4] who pointed out the importance of inspecting and touching the stump to indicate acceptance on the part of the doctor, and to push consideration of this part into the patient's consciousness.

The children and adults with amputations occurring after acquisition of a body-image has occurred, have a different problem. They now have an insult to their previously intact self-image and react to it accordingly. Two cases would serve to illustrate this point.

N. B. is a 9-year-old white female, referred to Newington Hospital from the Boston Children's Hospital, with lymphangioma of her right foot. The recommendation had been made in Boston that she be treated with an amputation because of problems connected with this foot. This lymphangioma was grossly evident at birth. She had surgery in the past for recurrent chronic infection of her foot and breakdowns of the overlying skin. The right foot was much larger than the left. She had to wear special shoes and was unable to participate in full physical activity because of the deformity. The child was interviewed prior to a below knee amputation. The focus of the effort was to explore her feeling toward the limb, the surgery and a prosthesis. In the process, she was able to establish a friendly relationship on which she could draw some support. This included a painstaking effort to detail the hospital procedure. There was close communication with the surgical staff during her hospitalization. She displayed a strong attitude of denial prior to surgery, evident in her drawings and interview behavior. After surgical recovery, she became spontaneous and open. Her parents were clearly supportive and felt comfortable in the management of the case.

R. R. is a 13-year-old white female, who was referred here this past June, with a three week history of pain in her right knee and X-ray evidence of an osteolytic lesion.* On July 7, 1961, an amputation of her right leg at the hip was undertaken under the added handicap that the surgical team was unable to use whole blood due to the religious beliefs of the parents. Post-operatively, she complained excessively of pain in her hip and the site of her amputation, yet presented a very stoic and superficially calm appearance on the ward. This was felt to be unusual and psychiatric consultation was requested. She was seen for a brief course of psychotherapy, during which time it became clear that she was vigorously attempting to suppress a grief reaction and had marked feelings of anger toward the medical staff. She also saw herself as a freak and was vehemently rejecting the idea of a prosthesis. In addition to her therapy sessions, she was also seen by the Occupational Therapy Department. She was clearly in conflict, having normal angry feelings at her loss, directed toward those who had taken her leg away, but was blocked in her ability to express the rage and grief she felt. In the Occupational Therapy shop she had the opportunity to channel her grief and anger into physical activity, which is a long accepted principle in psychiatric settings.

Once she had disposed of her angry feelings, she was able to invest in moving forward and was able to accept the idea of a prosthesis. She has since been fitted and is learning to walk reasonably well with a full leg prosthesis on the right.

Children's emotional reactions are hard to understand because they frequently express themselves in indirect ways. The important point to consider is that any patient will experience a period of grief and mourning[3, 8] following amputation. We must recognize mourning as a normal and necessary

* Microscopic diagnosis—Osteogenic Sarcoma.

adaptive process in which the patient "heals over" his psychic wounds. In this, there will be an inevitable sense of anger and rage at the loss, which is also part of the normal mourning process.

Adults who mourn exhibit symptoms of depression, which are clearly understood. Children, however, do not show such signs;[7] we see more often somatic symptoms, regression to more infantile levels, outbursts of temper and the like. In the case of R. R., this was the case, and one of the prime aids in the brief psychotherapy was to encourage verbal expressions of anger, as well as activity in her O.T. contacts, which could provide physical outlets for angry feelings. She was encouraged to pound in metal crafting, and pound she did. The prime block in her post-operative course appeared to be feelings of suppressed anger at her loss. The ease with which N. B. accepted her loss can be understood in view of the fact that she was able to view her limb quite directly as something undesirable and of negative value. An incidental finding in our discussion on the eve of surgery was that she fully expected to return from the operating room with an artificial limb attached firmly in place. If this belief were to have to have persisted, there may have been some unfortunate consequences. It certainly points out the need for detailed and repeated consideration with the patient of all stages of the surgical and treatment regime.

Both patients reported phantom limb sensations. R. R. reported the persistend feeling of "someone stepping on her toes," and N. B. reported a "tickling" sensation in the sole of her absent foot. This is an expected reaction to any amputation. Kolb[4] states, "The admission by the amputee of a limb phantom is the healthy psychologic response."

Phantom Limb

The phantom limb phenomena is of some interest and curiosity. The early medical literature made frequent mention of phantom limb phenomena, and most of the preoccupation has been with the physiological site of the process,[7] whether it was peripheral or central. Indeed, there is still concern on the neurosurgical services as to whether there is or is not nerve irritation at the amputation site. Levin[6] includes in his description a good discussion of the neurological basis for his views. The essence of this theory is the persistence of conditioned engrams in the appropriate brain centers to account for the phantom sensations. It may be said that the patient has suffered a loss to his already intact body-image. This central image persists, and some patients report that it may slowly seem as if the amputated limb is shrinking and becoming incorporated in the stump.[3]

The phantom phenomena are present in very young children. It appears that it is a function of the formation of the body image, which does take place in the second and third year of life. In direct support of this hypothesis is Easson's case of a 37-month-old child with a traumatic avulsion of the left arm and scapula, who had persistent phantom phenomena.[3] Simple phantom reactions are the rule. The patient may never mention them unless asked directly. Painful phantoms, on the other hand, are very rare, occurring in less than 1 per cent of the total cases reported.[1,4] Barring intercurrent organic physical deficits, it may be considered a prognostic sign of more serious underlying personality difficulty.[1,4] Kolb[4] reports that he has seen patients who have undergone singly and sucessively reamputation at higher levels, exploration of the stump, removal of the terminal neuroma, plastic operations on the stump, rhizotomies, sympathectomies, chordotomies, injection of alcohol into the neuroma, paravertebral anesthetic block of the sympathetic ganglia, spinal anesthesia and resection of the post-central cerebral cortex, and have been unrelieved of their painful symptoms. In a series of 27 cases, most of whom had come to the Mayo Clinic specifically because of phantom pain, Kolb[4] reported that after very careful physical, as well as emotional investigation, the reported pain appeared to represent an emotional response to the loss of an important part of the body, which had significance in terms of the body's relationship with others. Kolb[4] advocates early recognition of the painful phantom phenomenon and suggests supportive treatment before the pattern becomes crystallized and complicating factors, as narcotic addiction, interfere. His patients required less medication and had smoother post-operative courses as a consequence. The main focus of treatment is to fulfill the dependency needs, e.g. comfort and support, plus the opportunity for true communication to determine the patient's fears, anxieties and attitude toward the loss and deformity. Once it is established what the patient is trying to communicate, the course of treatment and dealing with the situation is often clearly indicated. For this reason, the adequate preparation of any patient for surgery, requires careful consideration of his emotional needs.

Psychological Considerations In Elective Surgery

Successful management of the congenital amputee would include early fitting, earlier than has been past practice, and we must consider more intensive supportive work with the parents of such children. We may also need to consider in children with congenital deformities requiring surgery, that such surgery should be done during the first year of life, if at all practical, in order to fit into the developing patterns of the body-image. If elective surgery cannot be done then, it should be delayed until the child is solidly entrenched in his own personality development. During the second and third year of life, his attachments to parents are too important and meaningful to be disrupted unless absolute necessity dictates. From the fourth to sixth years, the child acquires a heightened sense of genital or sexual differences and can readily interpret surgery as castration or potenial genital damage. Play therapy with children readily demonstrates this reaction, even in older children, and the consequences can be permanent, showing up in anxieties, phobias or behavior problems later.

The preparation of most children for surgery need not require the services of a psychiatrist. However, in order to prevent serious emotional reactions, the physician must take the required time to consider and work with the total child. At the time of stress when parents are most needed, they are necessarily excluded from the scene. The child needs to develop a temporary attachment to the doctor who will substitute for the missing parents. Under minor or major stresses, the child has come, of necessity, to depend on them for support and controls. He is simply unable to go through any major stress, such as anesthesia and surgery, without strong support and will undergo pathological reactions of major proportions if such support is not given. It is unwise to relegate such a major task to the paramedical and allied services without careful considerations.

I wish to emphasize that the major requirement is time. If the physician makes himself available to the child before and after surgery, a positive supportive relationship can occur. The model patient who is quiet and "no bother" may be depressed and sorely in need of help. All too frequently only the active, noisy child receives some attention, and then only to make him cooperate with the procedures and ward routines.

The basic objectives, in addition to the relationship, are to make the child as fully aware of the procedures as is possible. He should have a careful explanation of anesthesia induction, what to expect post-operatively, as well as repeated discussion of just what is going to be done. This can often be approached from the standpoint of the child, by asking him what he believes is going to happen. Distortions and misinformation can be exposed in this way. This will require repetition and painstaking attention to detail, including careful attention to what the child may hear on the ward during rounds or in the examining room. On one ward, though the patients regularly appeared disinterested, they would compare notes and searched the medical dictionary for what was discussed during the teaching rounds. Frequently an idea that the child may present as silly or inappropriate can be the most damaging. For example, an 8-year-old boy was subdued and overly quiet preceding surgery. In our contacts he revealed that his sister had died in her sleep some months ago. When he had been told, in lieu of more detailed explanation of anesthesia, he would be "put to sleep" for the surgery, he fully believed that he would also die as a consequence. The physician must be attuned to what the patient is communicating by his behavior, mood and symtomatology. For example, an outburst of anger may be an attempt to alleviate fear or anxiety.

Conclusion

The concept of body-image has not received much attention in considering a child's reaction to amputation, yet is a useful and workable way to consider the patient's reactions and attitudes. If a child has never had a fully intact body and is presented with a prosthesis during the critical stage when the "body-image" is forming, he will incorporate the limb into his use and action pattern. He then has a greater chance of becoming a "good user." If his amputation occurs later, he suffers an insult to a previously intact body-image and has to deal with feelings of loss before he can move on to higher levels of adequate development and adjustment.

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Surgically-Induced Disorders Of The Vocal Cords

John A. Kirchner, M.D.

■ Undesirable changes in pitch, volume, and resonance of the voice may result from injury to the laryngeal nerves during neck operations, particularly those on the thyroid gland, larynx, and hypopharynx. Other symptoms resulting from laryngeal nerve injury may include fatigability of the voice, aspiration of ingested liquids, and inability to cough effectively.

These unfortunate complications may occur even after the surgeon has taken particular pains to identify the recurrent and superior laryngeal nerves during the operation and feels certain that the nerves were not traumatized.

The usual explanation, particularly in a case performed under endotracheal anesthesia, is that there is some degree of edema in the larynx. If the voice improves after a few days, this reasoning is assumed to be correct and the surgeon concludes that no damage has been done. This explanation may not be correct, however, for temporary vocal disturbances resulting from incomplete or even complete interruption of the motor nerves may clear in a few days or weeks. Mirror examination of the larynx may even fail to disclose the real trouble, for it is not always possible to identify minor changes in motion or tension of the vocal cords by inspection.

How, then, can such vocal disturbances occur after careful dissection? How can they be avoided and what is the prognosis for return of function?

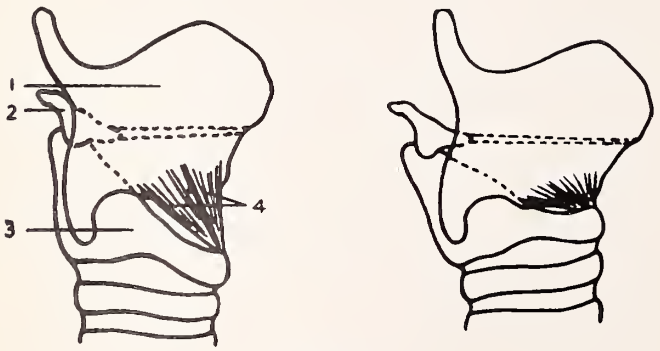

Figure I
Action of cricothyroid muscles on larynx. (Turner: Diseases of the Nose, Throat and Ear, John Wright and Sons, Ltd., Bristol, 1924.)

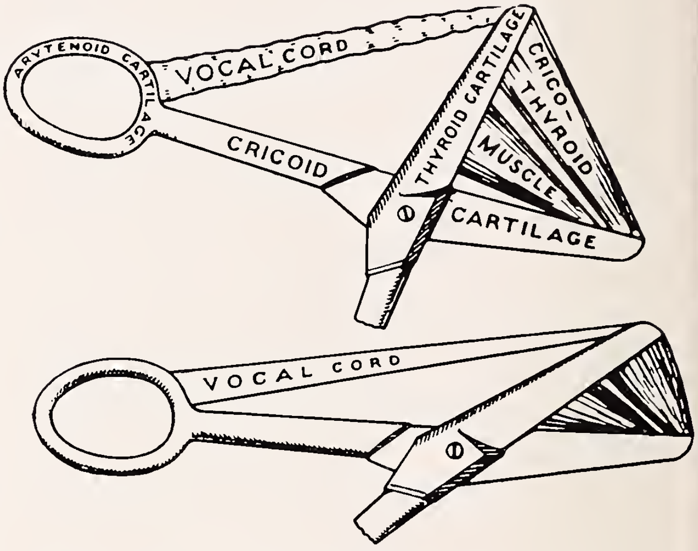

Figure II
Tensing action of cricothyroideus muscle on vocal cords. (Turner: Diseases of the Nose, Throat and Ear, John Wright and Sons, Ltd., Bristol, 1924.)

Nerve Supply

All the laryngeal muscles are innervated by the recurrent laryngeal nerve with one exception: the cricothyroideus, lying on the external surface of the larynx is innervated by the external branch of the superior laryngeal nerve. The interarytenoidius muscle gets its supply from both the right and left recurrent laryngeal nerves.

Movement of the vocal cord to the midline (adduction) and maximum movement away from the midline (abduction) are both mediated by the recurrent laryngeal nerve. Adduction is strengthened by the action of the superior laryngeal nerve on the cricothyroideus muscle, whose contraction serves three function:

a. Tension of the vocal cord by anterior elevation of the cricoid ring and posterior lowering of the cricoid plate.
b. Auxiliary adduction of the cords from the intermediate to the paramedian position because tension of the cords rotates the vocal processes inward.
c. Auxiliary abduction from the median to the paramedian position. (see Figures I and II)

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Sensation in the larynx above the cords is supplied by the internal branch of the superior laryngeal nerve, below the cords by the recurrent laryngeal nerve.

A denervated vocal cord may assume one of four positions:

1. Midline or completely adducted
2. Paramedian, with 3-5 mm. between the cords
3. Cadaveric, with about 7 mm. between the cords
4. Abducted

Injuries To The Nerves And Effect On Vocal Cords

Galen reported, aphonia as a result of sectioning the recurrent laryngeal nerve, and stated that the gradual return of vocal function after this incident was brought about by communicating branches between the superior and laryngeal nerves.[1] Martin, in 1734, drew the same conclusions in dog experiments.[2] This idea was challenged by the work of Lushka in 1871[3] and was definitely disproved by Lemere in 1934.[4, 5]

COMPLETE SECTION OF THE RECURRENT LARYNGEAL NERVE

Complete section of the recurrent laryngeal nerve is followed by median or paramedian position of the vocal cord of that side. With a cord in the paramedian position, unable to be brought fully into the midline, the patient is without voice. He can produce only a rough, weak noise and may complain of shortness of breath because of the escape of unused air through the open glottis. This vocal cord gradually resumes a midline position because of the tensing action of the unaffected cricothyroid muscle of the same side. (Figure III)

Arnold divides the vocal changes during recovery into five stages as the cord returns from the paramedian position to the midline.

1. Complete aphonia
2. Severe dysphonia
3. Flutter voice
4. Slight dysphonia
5. Fully compensated voice

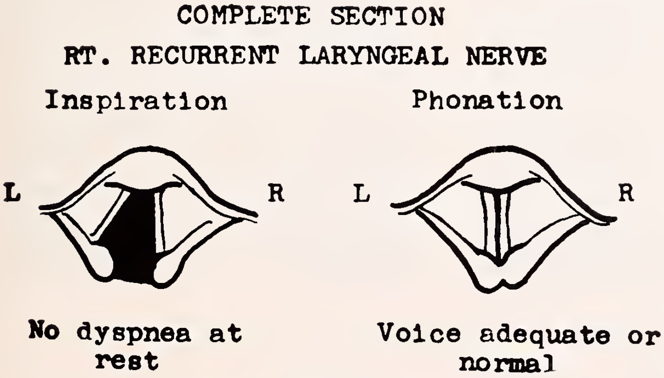

FIGURE III
Complete section, right recurrent laryngeal nerve, late.

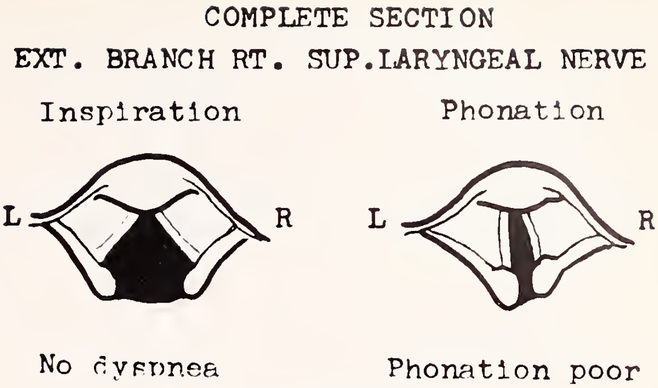

FIGURE IV
Complete section, right superior laryngeal nerve.

These stages may occur rapidly within a few days or may require a longer period of time.

COMPLETE SECTION OF THE SUPERIOR LARYNGEAL NERVE

Complete section of the superior laryngeal nerve results in paralysis of the cricothyroid muscle. As a result, the two vocal cords will occupy different levels, because the cricoid cartilage on the affected side is not elevated during phonation. In addition, the glottic chink will appear rotated, with the posterior commissure deviated to the side of the paralysis as a result of the rotating action of the normal cricothyroid muscle.

Vocal symptoms resulting from damage of the external branch of the superior nerve on one side are listed by Arnold as follows:[7]

1. Vocal weakness
2. Shortened phonation time as a result of air waste
3. Lowered speaking pitch
4. Reduction of vocal range
5. Loss of singing voice

Mirror examination shows, in addition to an oblique glottis, a shortened vocal cord, because the lack of tension allows the vocalis muscles to pull the arytenoid cartilage forward. Moreover, the affected cord, lacking tension, will be aspirated downward with inspiration and blown upward with expiration (Figure IV)

If the injury has occurred above the internal laryngeal branch, unilateral laryngeal anesthesia will be superimposed on the above findings.

COMPLETE SECTION OF BOTH THE RECURRENT LARYNGEAL AND SUPERIOR LARYNGEAL NERVES OF ONE SIDE

This results in an intermediate or "cadaveric" position of the affected cord, with bowing, flaccidity, and shortening of the cord, with a tilting forward of the same arytenoid. Because of the bilateral innervation of the interarytenoid muscles, no absolutely complete paralysis can be obtained from

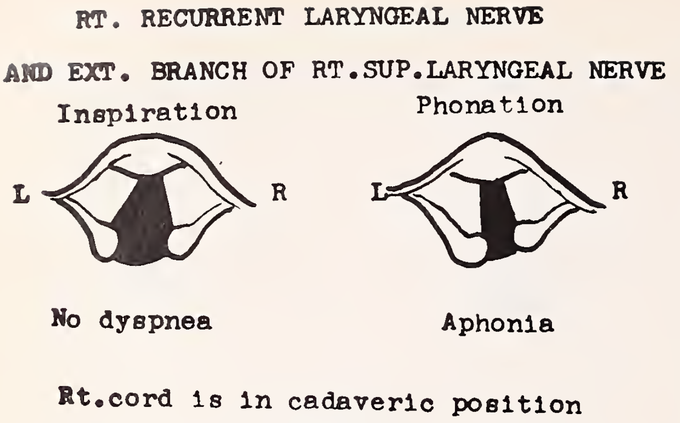
RT. RECURRENT LARYNGEAL NERVE
AND EXT. BRANCH OF RT.SUP.LARYNGEAL NERVE
Inspiration
Phonation
L
R
L
R
No dyspnea
Aphonia
Rt.cord is in cadaveric position

FIGURE V

Complete section of both the recurrent and superior laryngeal nerves of the right side.

unilateral nerve interruption. The patient has complete aphonia without dyspnea. Air loss with phonation produces shortness of breath. Patient is unable to cough effectively. If the nerve interruption has been high enough to include the internal branch of the superior laryngeal nerve, unilateral anesthesia of the larynx may result in aspiration of fluids. (Figure V)

While these general principles serve to explain most vocal disorders following injury to one or both of the nerves to the larynx, the problem is somewhat complicated by the possibility of partial, rather than complete, sections of the nerves, and by branching of the recurrent laryngeal nerve in the thyroid space before it enters the larynx.

R. L. Gregg, working with dogs, reported that the recurrent laryngeal nerve, when transilluminated in its lower portion, shows two main trunks within the sheath.[8] These trunks emerge, one to supply the cricoarytenoideus posticus, the powerful abductor muscle of the cords, the other to the cricoarytenoideus lateralis, the adductor. The adductor nerve was always larger than the abductor in his experiments.

Incidence

Injuries to the recurrent laryngeal nerve are usually unilateral. Bilateral injury to the recurrent laryngeal nerve results in severe respiratory obstruction, and, strangely enough, in little or no vocal disturbance after the initial dysphonia. since the cords assume a midline position.

Since Lahey's reports in 1938, routine nerve dissection has gained acceptance. Lahey reported an incidence of 0.3 per cent injuries after routine dissection, as compared to 1.6 per cent before.[9,10] Wade has reported a 5 per cent incidence of vocal complications,[11] Blomstedt and Rydmark report a 9.4 per cent incidence (56 of 593 cases).[12] Most of the cases in this latter series were operated upon under general anesthesia (471 of the 593).

Anatomic Reasons For Vulnerability

RECURRENT LARYNGEAL NERVE

There are two main groups: (1) variations in the relationship of the recurrent laryngeal nerve to the inferior thyroid artery, to the inferior thyroid vein, and to the gland itself;[13, 14, 15] and (2) branching of the recurrent laryngeal nerve before it enters the larynx.

Wade, in a study of 200 laryngeal nerves in 100 patients, found that 30 were vulnerable to injury, chiefly as a result of fixation of the nerve to the gland by an arterial fork.[11] His study showed six main relationships between the nerve and artery. (Figure VI)

Wade lists the causes of vulnerability as follows:

1. Displacement, as with asymmetrical growth in a nodular goiter.
2. Close relationship of the nerve to the glandular branches of the superior division of the inferior thyroid artery (Group 5, Figure VI). This is particularly dangerous with a vascular goiter, where multiple hemostats must be placed.
3. Fixation of the nerve to the gland by an arterial fork or by a fascial envelope of the thyroid gland when well developed and containing the nerve. The closer the inferior thyroid artery divides to the gland, the greater is the danger to the nerve. (Group 4, 5 and 6, Figure VI).
4. Tunnelling. Occasionally occurs with nodular or diffuse toxic goiters. It is usually associated with arterial or fascial fixation. (Figure VII).

Wade estimates 5 per cent injuries to the nerve and points out that unless routine post-operative laryngoscopy is performed, an injury will likely remain undetected, since the voice tends to improve in time after unilateral injury.

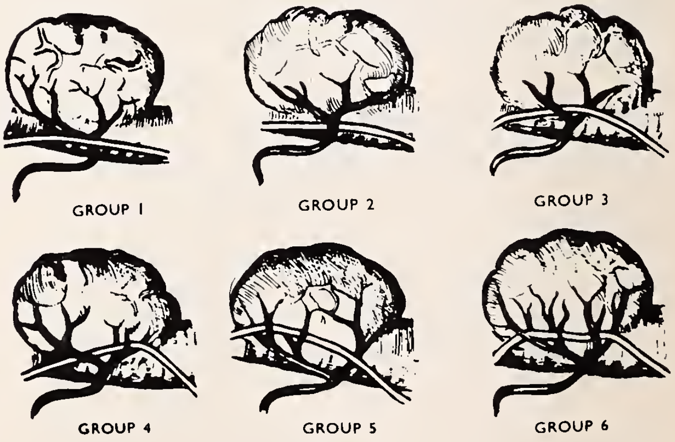

FIGURE VI

Six relationships between recurrent laryngeal nerve and inferior thyroid artery. (Wade, 11.)

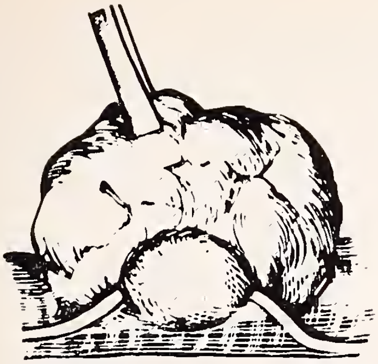

Figure VII

Tunnelling, or enclosure of the nerve by a thyroid nodule. (Wade, 11.)

Table I
Relationship of Recurrent Laryngeal Nerve to Inferior Thyroid Artery

	Fowler and Hanson[13]	Armstrong and Hinton[14]	Reed[15]
Number of dissections	(400)	(100)	(506)
Nerve posterior to artery	66%	43%	39%
Nerve anterior to artery	26%	34%	19%
Nerve passes between main branches of artery	8%	23%	22% (etc.)

In addition to these causes listed by Wade, another cause of vulnerability is extra-laryngeal division of the recurrent laryngeal nerve. This was established by the work of Meckel in 1832,[16] yet was scarcely mentioned in the literature of the following hundred years. Recent reports have pointed out the high incidence of extralaryngeal branching of the recurrent laryngeal nerve, 73 per cent in a series studied by Armstrong and Hinton,[14] (see Table I). Morrison states that the recurrent laryngeal nerve divides in the thyroid space in 43 per cent of the adult humans.[17] (Figures VIII, IX)

On the basis of his work described above, R. L. Gregg states that injury to one or the other trunk of a simply-branched nerve will produce a pure abductor or pure adductor paralysis. Injury to a secondary or tertiary division of the recurrent laryngeal nerve in the thyroid area could, then, account for the complex type of paralyses sometimes seen. (The evidence for such a separation of the adductor and abductor fibers in the recurrent laryngeal nerve of man is very meagre. In fact, several careful studies have produced evidence that the medially-directed branch is primarily afferent.)

SUPERIOR LARYNGEAL NERVE

The superior laryngeal nerve is vulnerable to injury because of its close relationship to the superior thyroid artery.[18] The external branch of the superior laryngeal nerve descends vertically on the outer surface of the inferior constrictor muscle and crosses the superior thyroid artery on its deep side as it approaches the cricothyroideus muscle. (Figure X). Moran and Castro reported eight cases of adenomatous goiter in which the superior laryngeal nerves external branch was purposely traumatized with a hemostat. All eight patients had post-operative vocal disturbances of varying durations.[19]

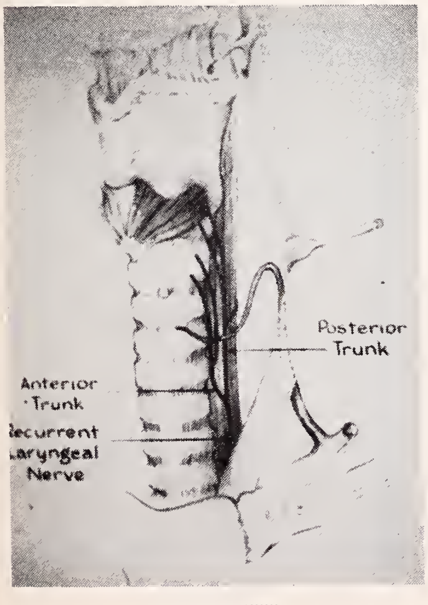

Figure VIII

Extra-laryngeal branching of the recurrent laryngeal nerve. (Morrison, 17.)

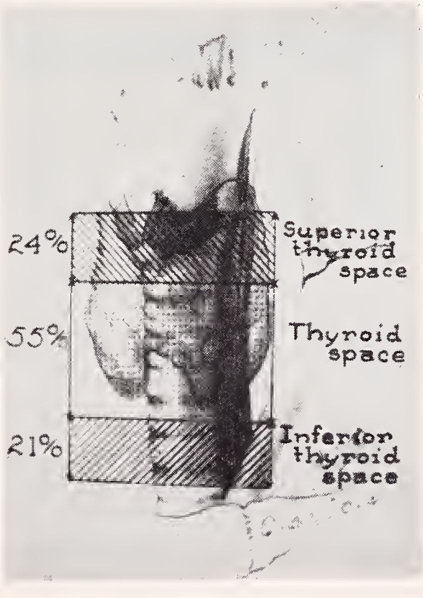

Figure IX

Location of the divisions of the recurrent laryngeal nerve. (Morrison, 17.)

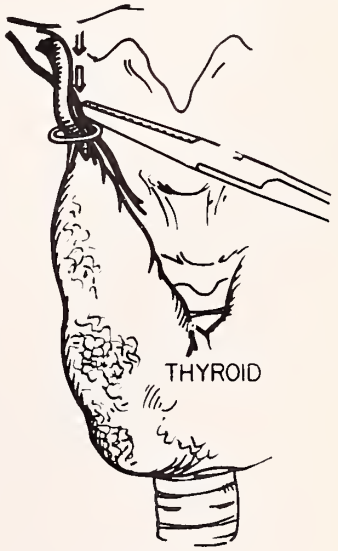

Figure X

Relation of superior laryngeal nerve (external branch) to the superior thyroid artery. The ring indicates where clamping of both structures can occur. (Moran & Castro, 19.)

Type Of Injury

Judd and his associates studied the effects of various types of injury to the recurrent laryngeal nerve in dogs.[20] The conclusions they reached seem reasonably applicable to man.

1. Crushing: This can occur if hemostats are placed along the proposed line of resection of the thyroid lobe, or if small bleeders are picked up along the lateral wall of the trachea. This injury may be temporary, but if a ligature or suture is then applied, the resultant damage may be permanent. Under local anesthesia a clamp may be removed immediately if a patient's voice changes.
2. Compression in a ligature. This may occur if the cut surface of the thyroid remnant is sutured.
3. Division by a sharp instrument. This can occur during resection of a gland, or with division of the inferior thyroid vein. About 2 per cent of recurrent laryngeal nerves leave the thorax anterior and parallel to the trachea, intimately related to the inferior thyroid vein. (Figure XI)
4. Stretching. While the gland is being displaced forward prior to removal. It is worse with substernal extension, but must be severe and prolonged to produce permanent injury.
5. Ischemia following exposure of the nerve.
6. (5 and 6 are "most exceptional" provided that the nerve is not roughly handled.)

Prognosis

Blomstedt and Rydmark succeeded in following the course of 53 of the 56 cases of post thyroidectomy paralysis.[12] In 21 there was full recovery, in 26 complete permanent paralysis resulted. In the remaining six, a partial paralysis continues. In no case was there any improvement after seven months.

Other authors are in general agreement on the prognostic value of the position of the paralyzed vocal cords. The midline paralyzed cord usually remains in this position. The paramedian position of the cord usually changes to a midline position in a few days or weeks. The cadaveric position is usually permanent.

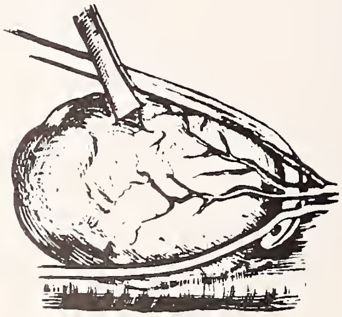

Figure XI

Approximately 2% of recurrent laryngeal nerves leave the thorax anterior to the trachea, paralleling the inferior thyroid veins. (Wade, 11.)

Prevention

Identification of the main trunk of the recurrent laryngeal nerve in the inferior thyroid space before proceeding to the gland is advisable and should keep injuries to a minimum. The superior laryngeal nerve can be protected by avoiding traction on the upper pole, and by adequate exposure and by individual ligation of the superior thyroid artery and vein.

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"Refractory" Ascites Of Cirrhosis: Newer Therapeutic Procedures

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■ The management of marked ascites, particularly in cirrhotic patients, creates a distressing problem to the physician and the patient, alike. In some of these patients, relief may be obtained with the usual measures, i.e., low sodium diet, bed rest, and the presently available diuretics, such as the mercurials, the chorothiazides, the hydrochlorothiazides and the chlorthalidones. The majority of these patients, however, are so resistant to these conventional measures of therapy that they themselves ask for abdominal paracenteses. Despite the fact that the clinician hesitates to perform repeated paracenteses because they deplete the body of protein and electrolytes and may precipitate hepatic coma[1,2,3] he may be forced to perform such procedures in these refractory cases so as to relieve them of abdominal discomfort and, often times, of respiratory distress.

Several approaches are recommended in cases of intractable ascites. Some are surgical, like the portocaval shunt and the double shunt operation,[4]—which while useful, have a high mortality and may precipiate porto-systemic encephalopathy or chronic neuropsychiatric disorders[5]—and bilateral adrenalectomy, which has been performed in only a few cases.[6,7,8] Others are medical, like infusions of dialyzed autogenous ascitic fluid[9] of calcium gluconate[10] or of salt free albumin[11,12] or administration of steroids,[13,14] alone or in conjunction with various diuretics.

Besides giving inconsistent and unsatisfactory results, most surgical and medical measures have been associated with various side effects which at times are serious and life endangering. The sequelae of the shunt operations and bilateral adrenalectomy, e.g., porto-systemic encephalopathy and Addisonian state respectively, have already been alluded to.[5,6,7,8] The infusion of dialyzed autogeous ascitic fluid carries with it the hazard of pyrogenic reactions, besides the poor diuretic response.[9] The diuretic effect of I.V. calcium gluconate is of only short duration since patients become refractory after repeated infusions, although the naturetic effect can be restored by small doses of a glucocorticoid.[10] The administration of salt-poor human albumin while equivocal and inconstant in the experience of several investigators[11-16] and also our own, may lead to cardiovascular complications. Similarly, administration of steroids may result in ulcer formation and bleeding, among other undesirable effects. Finally, besides the variable and unpredictable response of the various diuretics, hypochloremia and particularly hypokalemia with coma occasionally ensues[17,18,19] during their administration.

The causes of ascites in cirrhosis are still not completely understood. However, the finding of a low sodium content in the urine, saliva, sweat and feces of patients with ascites[20] and the finding of an increased excretion of aldosterone[21] had incriminated the latter as an important agent in the retention of fluid in cirrhotic patients. This hypothesis was confirmed by the results of bilateral adrenalectomy[6,7] and the suppression of aldosterone secretion by amphenone.[22]

The establisment of aldosterone as an important factor in the water retention of patients with cirrhosis of the liver, by its effect on the sodium reabsorption by the renal tubule, suggested a search for antagonists to this substance. In 1957, Kagawa and the co-workers reported on the synthesis of an aldosterone antagonist[23] and shortly thereafter, Liddle et al, reported on its clinical application with good results despite some side effects.[24,25] It was not, however, until recently that an improved, more potent derivative of these steroidal lactones was introduced which could be used orally and

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which while being very useful clinically in cases of intractable ascites had little or no side effects.[26,27] Spironolactone (Aldactone) was found particularly effective when combined with a thiazide and/or prednisolone.[28]

Because of the above reports, we set up a study on a group of cirrhotic patients with marked ascites who had not responded to any previous medical management.

Materials And Methods Of Study

Only thoses patients with cirrhosis (confirmed by clinical and biochemical* and occasionally histological data) whose ascites had been resistant to the conventional measures of therapy, such as low salt diet, mercurial diuretics and one of the thiazides, 50-150 mg. of hydrochlorothiazide or 5-10 mg. of bendroflumethiazide, have been selected for this study. All of these patients had received other forms of diuretics prior to their hospitalization.

The patients were placed on a diet containing approximately 200 mg. of sodium. They also received potassium chloride supplements of 3 gms. daily. The fluid intake was not restricted. Initially, a 24 hour urine specimen for determination of sodium, choride and potassium was obtained and serum electrolytes were drawn for control. The patients then received at first, hydrochlorothiazide, 300 mg. daily (in three divided doses) for a period of five to seven days. If there was no satisfactory response with regard to weight loss, urinary output,

TABLE I

CHANGES OBSERVED ON ADDITION OF SPIRONOLACTONE TO BENZYDROFLUMETHIAZIDE IN CIRRHOTICS WITH ASCITES WHO WERE NOT DIURESING ADEQUATELY ON BENZYDROFLUMETHIAZIDE ALONE

QUANTITIES MEASURED AND COMPARED	BASE LINE			CHANGE OBSERVED			
	NUMBER OF CASES PERTINENT	MEAN VALUE	STANDARD DEVIATION OF VALUES	MEAN CHANGE*	STANDARD DEVIATION OF CHANGE	SIGNIFICANCE OF CHANGE	
						T	P
Body weight on day Spironolactone started.	21	71.7 kg. (158.1 lb)	16.5 kg. (36.3 lb)	—	—	—	—
Average rate of weight changes*; prior 4 days vs. 1st 6 days† of Spironolactone.	21	−141 gm. per day‡ (−0.31 lb per day)	281 gm. per day (0.62 lb per day)	−467 gm/day (1.03 lb/day)	381 gm/day (0.84 lb/day)	5.6	$<.001$
Average urine volume; prior 4 days vs. 1st 6 days of Spironolactone.	22	1373 ml/d	437 ml/d	384 ml/d	288 ml/d	6.2	$<.001$
Urinary electrolyte excretions, single determinations; within prior 4 days vs. 6th, 7th, or 8th day of Spironolactone.							
Sodium	15	37.8 mEq/day	34.7 mEq/day	69.8 mEq/day	75.1 mEq/day	3.6	$<.01$
Potassium	15	51.1 mEq/day	32.4 mEq/day	−5.0 mEq/day	40.0 mEq/day	.5	$>.50$
Chloride	15	67.5 mEq/day	45.6 mEq/day	44.3 mEq/day	55.0 mEq/day	3.1	$<.01$

* A negative sign means a tendency to decreasing values with time.

† In one case average was for 1st 5 days only.

‡ This tendency to weight loss prior to Spironolactone therapy when tested for statistical significance showed: $t = 2.3$, $p < .05$.

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* Biochemical determinations included concentration of serum bilirubin albumin, globulin, gamma globulin, cholesterol, cholesterol esters, alkaline phosphatase, cephalin flocculation, thymol turbidity, glutamic-oxalacetic and glutamic pyruvate transaminase and isocitric dehydrogenase.

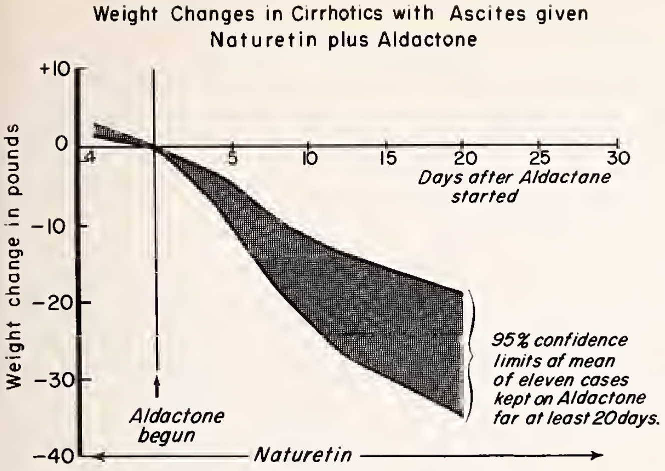

FIGURE I

Showing weight changes in cirrhotics with ascites given benzydroflumethiazide (Naturetin) plus spironolactone (Aldactone).

and decrease in the ascites, 400 mg. of spironolactone (in four divided doses) was given in addition to the above. If no satisfactory response was obtained with these two substances in one or two weeks, prednisone, 30 mg. daily (in three divided doses) was added. The body weight and the 24 hour urine volume were recorded daily. The 24 hour urinary excretion of sodium, chloride, potassium as well as the serum sodium, chloride and potassium were determined before, during and after each course of treatment, or at weekly intervals.

Twenty-five cirrhotic patients (sixteen males and nine females) with their ages varying from 27 to 70 years fulfilled the criteria for the selection of patients and are reported here.

Of these twenty-five patients, five received only hydrochlorothiazide, 300 mg. daily; fourteen required a combination of spironolactone, 400 mg. and hydrochlorothiazide 300 mg. or bendroflumethiazide, 30 mg.; and six patients required the combination of hydrochlorothiazide or bendroflumethiazide with sproinolactone and prednisone. The total duration of treatment ranged from one week to forty-seven days. In a few instances of very severe ascites, spironolactone was started simultaneously with the thiazide compound in order to give the patient faster relief.

Results

The above regimen gave a satisfactory response in all except two cases. There was a definite weight loss

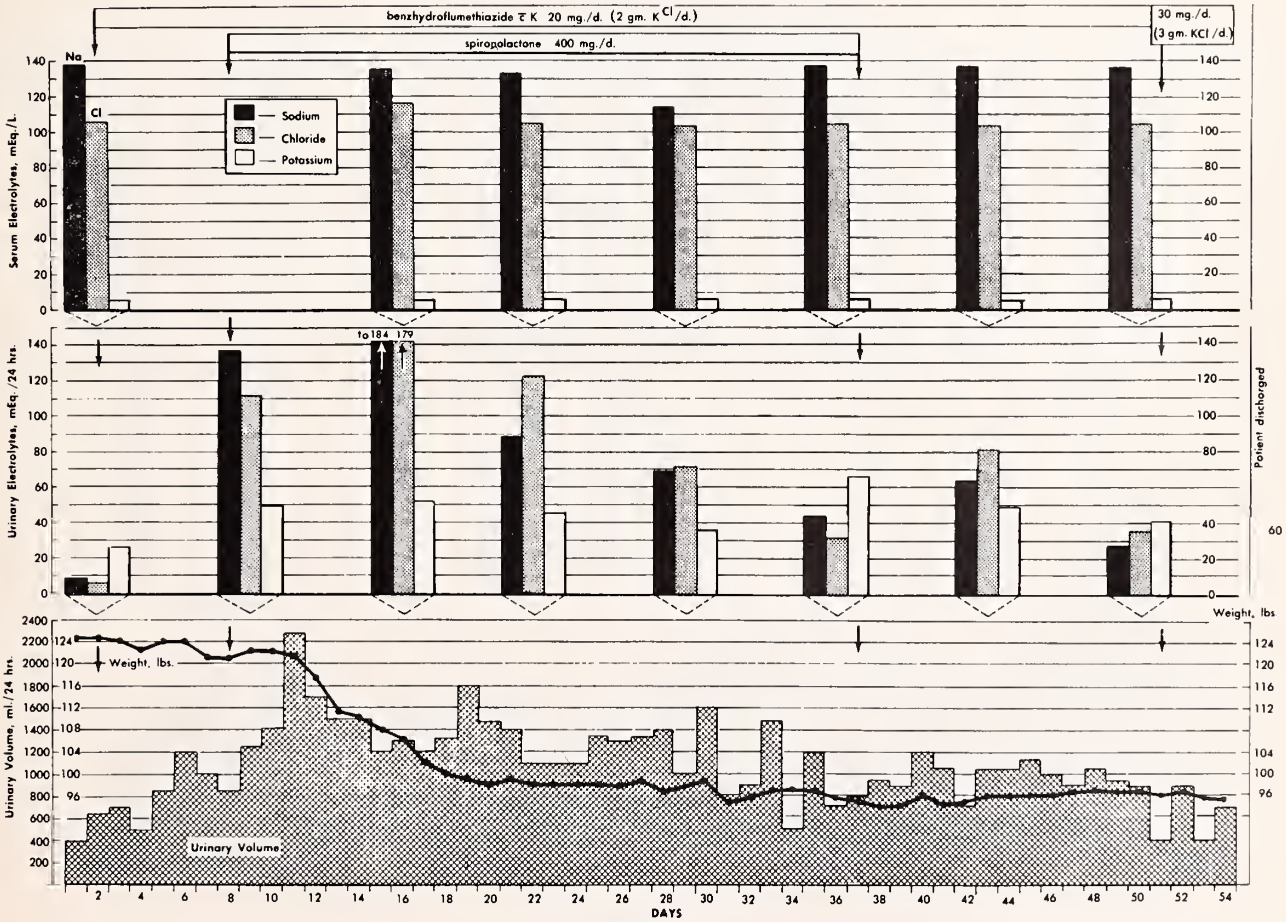

FIGURE II

Showing marked weight loss and increased urinary excretion of sodium and chloride following the administration of benzydroflumethiazide and spironolactone.

and increase in the twenty-four hour urinary output (Table I) (Figure I). There was also a noticeable decrease in the ascites and edema in all of them, while in five cases, the ascites had completely disappeared at the end of the treatment.

Of sixteen patients who manifested leg edema of 4+ to 1+ prior to treatment, all except two showed complete subsidence of the edema after treatment. The two patients who did not have a satisfactory clinical response to therapy, showed nevertheless, a marked increase in urinary excretion of sodium. In one of them, the dose of spironolactone was raised up to 800 mg. per day for one week without much effect.

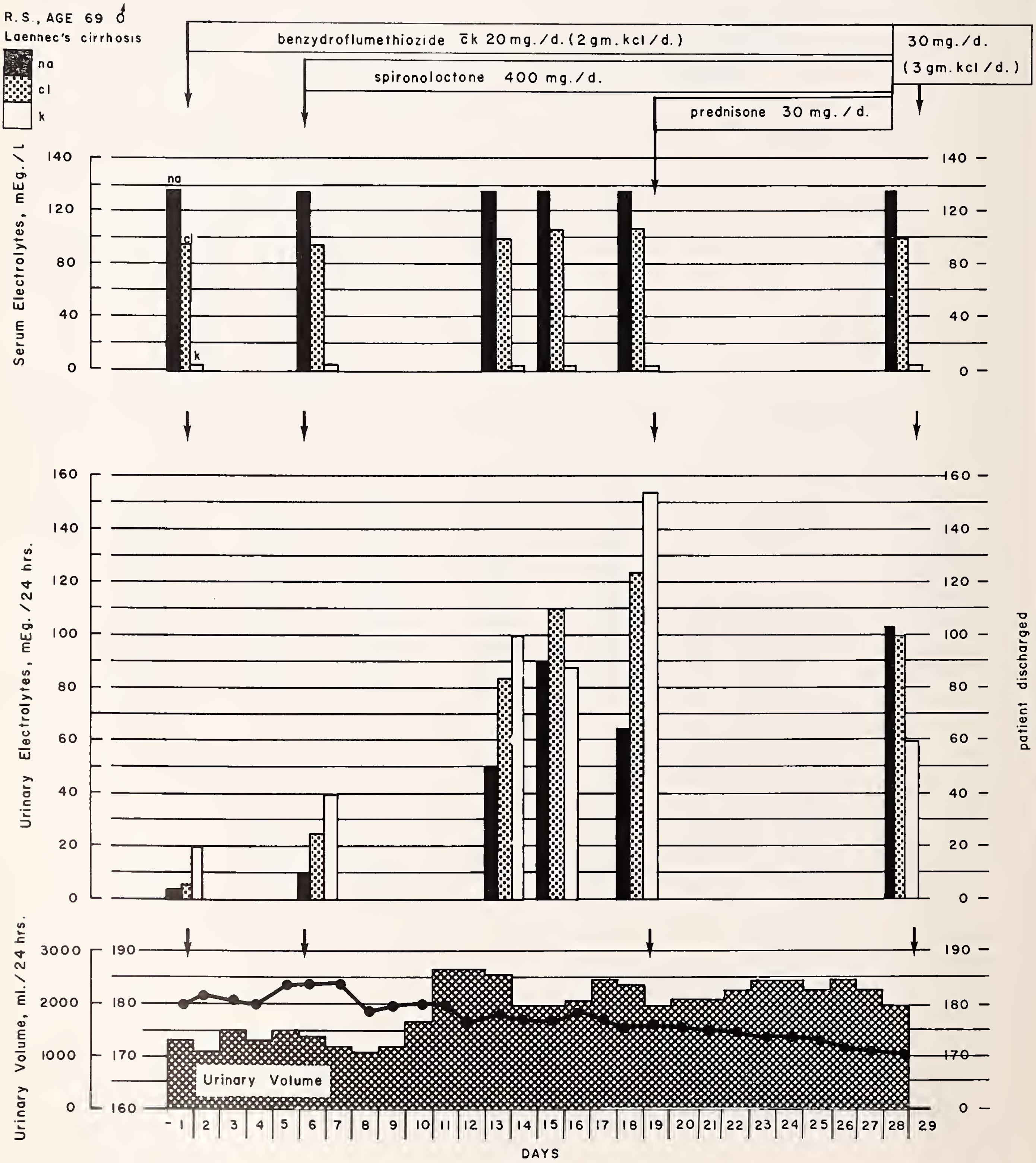

Figure III

Showing an increased output of sodium following the administration of prednisone.

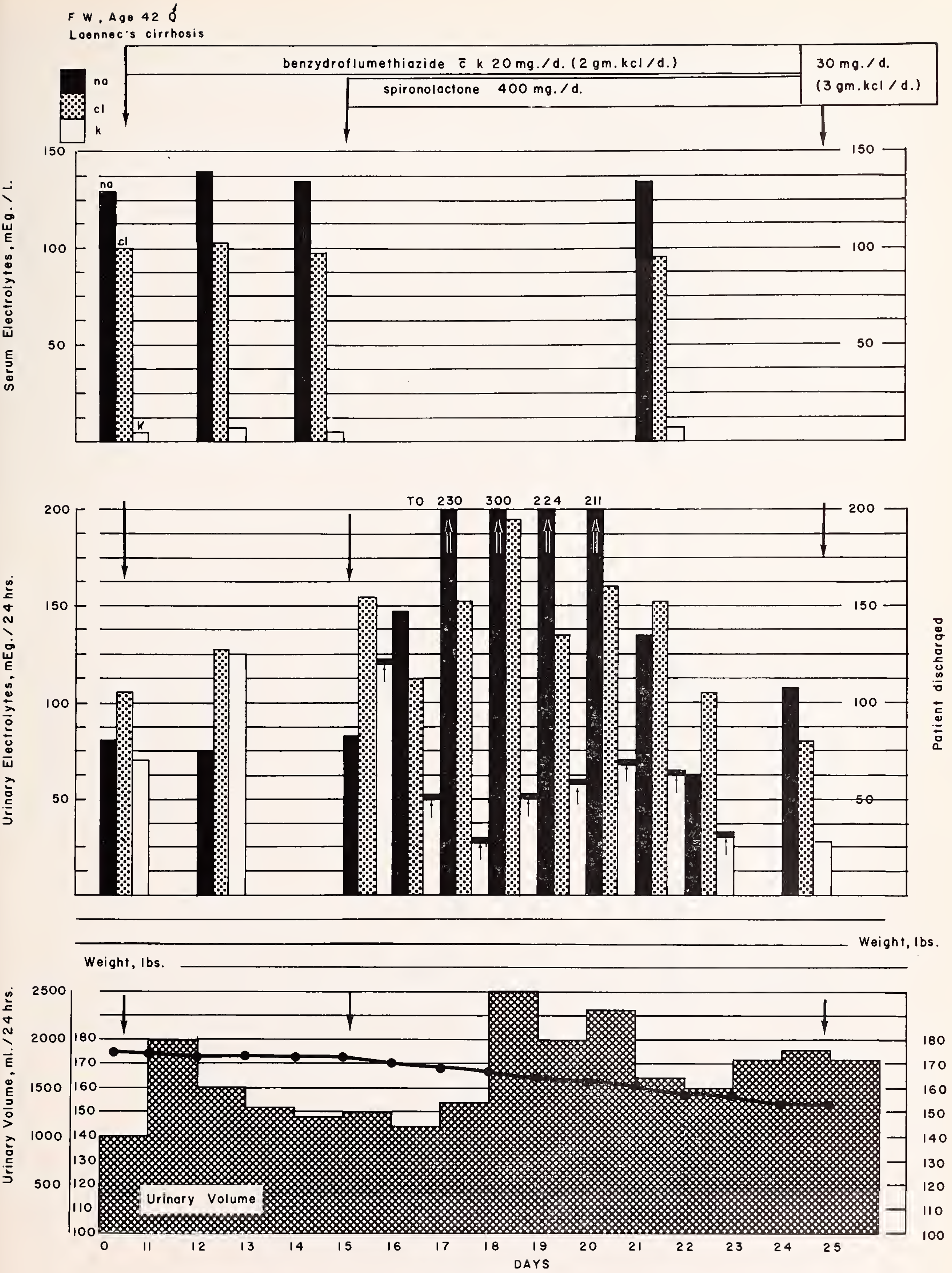

Figure IV

Showing the marked diuretic and saluretic effect of spironolactone two days after its administration and persisting for four days when it gradually begins to become less effective.

Electrolyte Changes Before And After Treatment

All, except four patients, showed an increase in the 24 hour urinary excretion of sodium and of chloride (Table I). In two cases however, there was a decrease in the chloride output of 13 and 33 mEq respectively. Urinary excretion of potassium increased during the period of thiazide medication alone, but dropped after the administration of spironolactone.

The combination of a thiazide and spironolactone caused a marked urinary excretion of sodium as well as a good clinical response (Figure II). In some patients, a more satisfactory clinical response was obtained with a combination of a thiazide, spironolactone and prednisone. In them, the urinary excretion of sodium was also higher (Figure III).

A combination of a thiazide and prednisone given to two patients, did not show a good therapeutic effect until spironolactone was added, when a maximum response was obtained.

In one cases, spironolactone was given initially, but showed no effect. After the addition of 300 mg. of hydrochlorothiazide, a marked diuretic and even more marked saluretic effect wes noted.

As a rule, hydrochlorothizide, 300 mg. or 20 mg. of bendroflumethiazide plus spironolactone, 400 mg. produced within two to three days, a good diuretic response which continued more or less evenly as long as the medication was continued. The diuretic effect and the weight loss were matched by the marked saluretic effect, the urinary output of sodium and chloride becoming 10-20 fold the premedication period (Figure II). The output data presented in this graph however, do not give a completely true picture of the saluretic effect since the urinary electrolytes after seven days of treatment may not represent the actual increase in excretion of sodium and chloride. This hypothesis was confirmed by daily determinations of urinary electrolytes in a couple of patients. Figure IV shows a representative case in which the highest output of

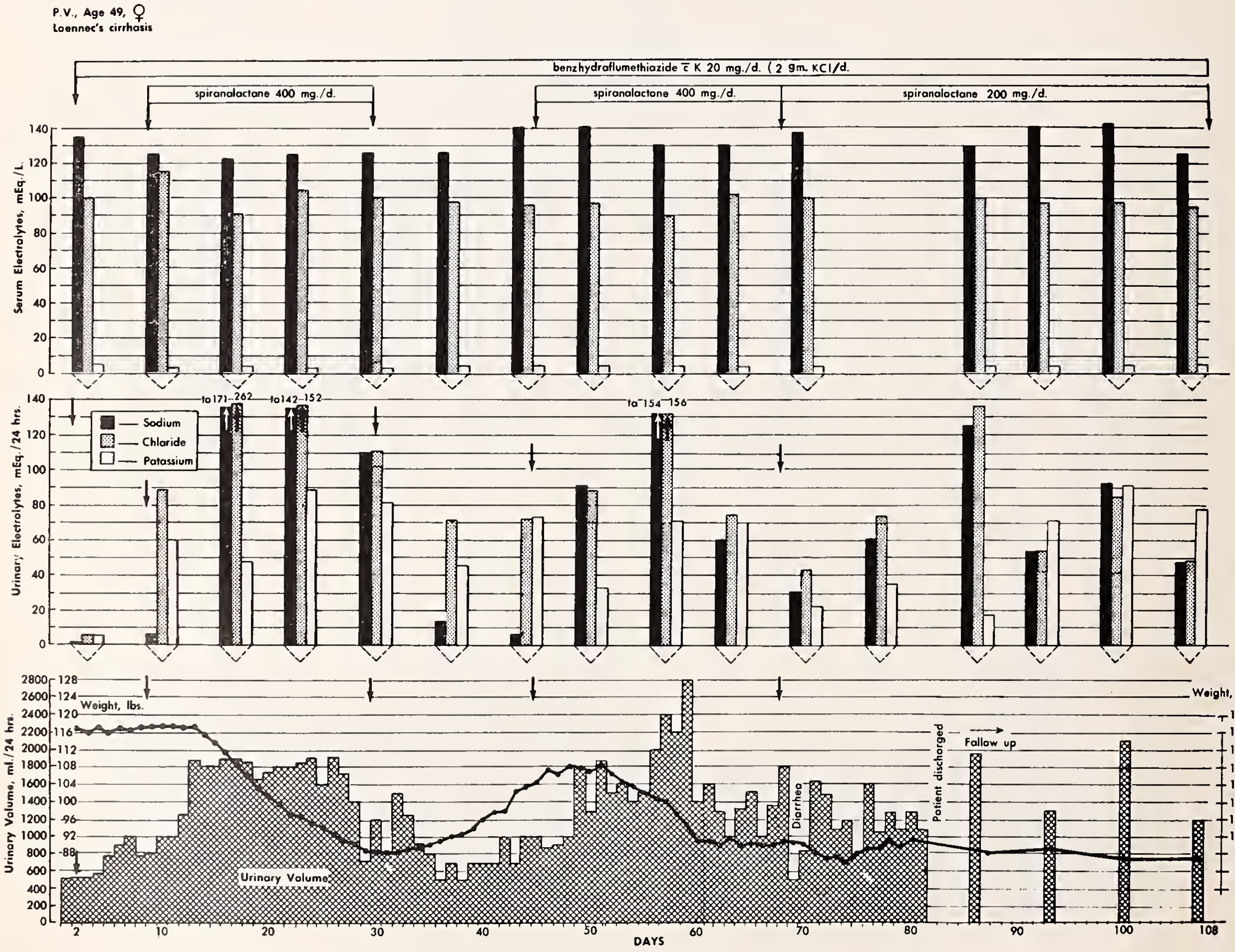

Figure V

Showing the marked response to spironolactone and gradual return of edema and decrease of urinary electrolyte excretion shortly after cessation of spironolactone administration. It also shows the improvement soon after spironolactone is started again and maintenance thereafter on a smaller dose (200 mg.).

sodium is noted from the third to the sixth day with markedly lower values on the seventh day. Technical difficulties however (personnel and space) prevented us from doing daily determinations on all patients.

While the patients continued to keep their weight on a horizontal level once they reached the so-called dry stage, there was a gradual diminution in the urinary excretion of sodium and chloride even while the patients were still on spironolactone. After the latter was discontinued, the weight and urinary output remained the same in some, while in others (five cases) a gradual increase in weight and decrease in urinary output and sodium ensued (Figure V). After restarting the spironolactone there was again marked weight loss and increase in urinary volume and output of urinary electrolytes (Figure V). This was observed in five cases. In three patients, the dose of sprionolactone could be reduced to half of its original amount without greatly disturbing the patient's urinary volume or electrolyte excretion (Figure V). Maintenance of the appropriate weight level and hydration was possible in nine other patients with 30 mg. of bendroflumethiazide daily.

All of these patients except one were spared from abdominal paracentesis during the period of observation.

Twelve patients of this group have been followed in the outpatient clinic and appeared to be doing well.

The serum electrolytes of these patients decreased slightly during the treatment. One patient showed a low serum sodium and choride initially, but did not manifest the clinical symptoms of hyponatremia. Moreover, despite an increase in urinary excretion of sodium after spironolactone the serum level spontaneously increased towards the normal level. Only one patient (Case 12) showed a decrease in serum sodium and chloride while on treatment to as low as 123 mEq/l and 87 mEq/l respectively, but remained clinically unchanged. These values returned gradually to normal levels after the thiazide compound was discontinued; they did not neccessitate the administration of hypertonic saline solution.

Discussion

The above observations indicate that by using various combinations of "diuretics" one can control, in most instances, even the previously so-called "intractable" ascites of cirrhotic patients. Hence, one can now avoid frequent abdominal paracenteses or other measures which were mostly of temporary benefit but, in some instances, associated with prolonged side effects. As our study progressed, we were also favorably impressed with the fact that some patients could continue the above outlined therapeutic regimen for many weeks without any apparent side effects or decrease in effectiveness. In most instances however, it was possible to eliminate first, one of the substances, e.g., prednisone, then the other, e.g., spironolactoue, and to continue on the thiazide only. In a couple of cases, the thiazide dose too, could be decreased without any untoward effect, the patient continuing to maintain himself at a "dry" level on an outpatients basis.

The absence of any side effects from the drugs themselves or from the possible changes in the biochemical architecture makes this regimen an important milestone in the treatment of cirrhotic patients with "refractory" ascites. This regimen obviates the necessity of prolonged hospitalization of these patients who previously required many weeks of hospitalization and later, after discharge, frequent returns for abdominal paracenteses. The use of these substances may in some instances also help in the preparation of a more palatable diet for these patients, since in view of the marked saluretic effect produced by the above combinations, the salt content of the diet would not have to be too rigidly controlled. In many instances, patients with cirrhosis fail to consume the required caloric amount because of the "poor" taste of their diet. A somewhat less rigidly controlled salt content of the diet will improve its taste and thus lead to better nutrition.

Summary

In a group of 25 patients of cirrhosis of the liver with so called "intractable" ascites, a regimen of large doses of a thiazide compound, plus spironolactone, proved effective in decreasing or eliminating the ascites and edema. In a small number of cases, the addition of prednisone to the above regimen was necessary for obtaining clearance of the ascites. The patients tolerated this regimen well and showed no significant side effects. Most of the patients could be followed on an outpatient basis after they were discharged from the hospital.

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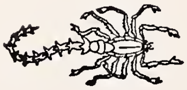

Epidermoid Carcinoma Of The Anal Canal And Perianal Skin

Paul G. Kuehn, M.D., John F. Reed, M.D., George B. McAdams, M.D.

■ Epidermoid carcinoma involving the perianal skin and anal canal is a rare lesion. The location of the lesion in an inaccessible and poorly visualized anatomical area leads to late or unsuspected diagnosis of a potentially lethal disease. This is in contrast to epidermoid carcinoma of the lip where the lesion is easily visualized anatomically and has a good prognosis with surgical or radiation therapy.

This study concerns 30 patients diagnosed and treated for epidermoid carcinoma of the perianal skin or anal canal since 1938 at Hartford Hospital. Twenty-six consecutive patients were available for five years' follow-up and evaluation. Other studies concerning this type of cancer have been done in the past.[2, 6, 7, 18, 20]

In our study, 16 of the tumors were in men and 14 were in women. A greater incidence in females is reported in other series.[10] The youngest patient was 40 years of age and the oldest, 85 years. There was no direct correlation between the size of the lesion and the severity of the disease. One patient with a 1 cm. ulcerated "hemorrhoidal tag" had advanced disease with a pathologically proven inguinal node metastasis. The gross lesions measured 1 cm. to 6 cm, in diameter and involvement of contiguous structure was frequent. There were four patients who had direct involvement of the posterior vaginal wall with tumor.

Pain and bleeding were the most common symptoms, although pruritis and the feeling of a lump at the anus were sufficiently frequent to warrant mention.

Errors in diagnosis were frequent. Seven patients had surgical procedures performed (hemorrhoidectomy, fistulectomy, or excision of anal ulcers) for what was considered benign disease. The surgeons were unpleasantly surprised by the pathologists' report. Five patients had prolonged treatment by their local physicians for six months to two years (cauterization, treatment with salves, sitz baths, etc.) prior to diagnostic biopsy or excision. Because of this, early biopsy or excision of any suspicious lump or ulceration in the anal canal and perianal skin should be done; and all excised tissue, including hemorrhoids, should be submitted for pathological study.

The differential diagnosis of lesions in this area should include epidermoid carcinoma, hemorrhoids, condylomata, chancroid, melanoma, lymphopathia venerium, lymphosarcoma and tuberculosis.

Anatomy

The exact anatomic location of the tumor should be defined so that selected methods of treatment can be used. The anatomy of the anal canal has been extensively studied and is well documented in the literature.[1, 3, 8, 9, 12, 14, 19] Figure I demonstrates the essential anatomy. In this study, only the patients with epidermoid carcinoma arising primarily from the perianal skin and anal canal (from the anal verge to and including the mucocutaneous

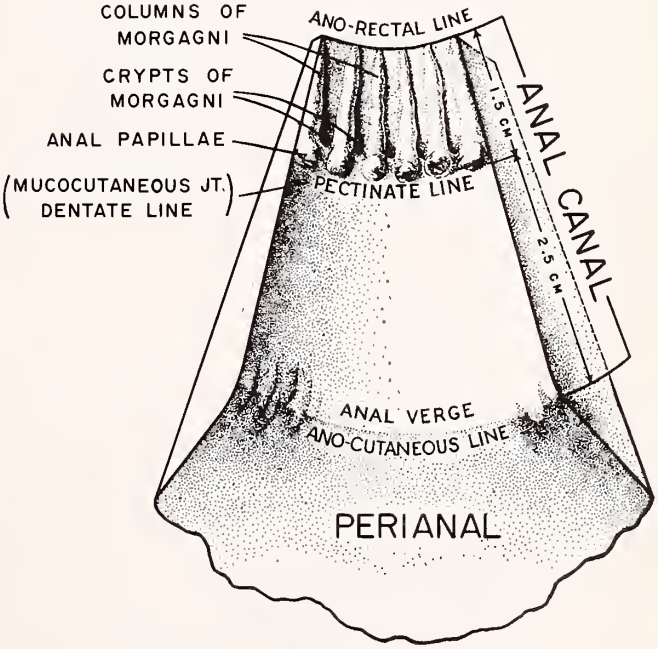

FIGURE I
Anatomy of the anal canal and the perianal skin.

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junction or pectinate line to the anorectal line) are included. It should be noted that the anal canal extends upward for a short distance beyond the mucocutaneous junction.

Lymphatic Drainage

The lymphatic drainage of the anus has interested anatomists in the past.[4, 15, 16] There are three lymphatic trunks that drain the anorectal area. The inferior collecting trunks originate in cutaneous part of the anus and empty into the superficial inguinal nodes. The middle collecting trunks, comprising the middle hemorrhoidal and laterosacral lymphatics, terminate in the hypogastric or lateral sacral nodes and in the nodes of the promontory. The superior collecting trunks or superior hemorrhoidal lymphatics, whose origin may extend as low as the anal cutaneous zone, terminate in the lymphoid aggregation at the level of the bifurcation of the mesenteric artery.

Pathology

Epidermoid carcinoma of the anus is histologically similar to epidermoid malignancies elsewhere. The majority of the tumors in this series (28 patients) were well-developed squamous cell carcinomata with moderate anaplasia and metastatic activity accompanied by varying degrees of invasion into the surrounding tissue of the anal canal and perianal skin. Pearl formation was abundant. Many of the nests and strands of malignant cells, however, appeared smaller, contained nuclei darker than ordinary squamous cells, and resembled the transitional cell type; such as is often encountered in cancer of the cervix.

Highly undifferentiated tumors were rarely encountered in the primary tumors; yet, pathologically proven metastases in the nodes occurred in greater than 50 per cent of the patients. Only one of our patients was of the basaloid variety who succumbed to a coronary occlusion 20 years after treatment without recurrence.

It has been previously reported that epidermoid carcinoma can also occur elsewhere in the colon. Keyes[11] reported a patient with tumor in the descending colon and Cattell and Williams[6] found a similar tumor in the rectosigmoid.

Method Of Tumor Spread

An attempt was made here to analyze operative specimens and autopsy material for size of lesion, anatomic location, presence of local infiltration and lymphatic and hematogenous metastases. It soon became apparent that local infiltration and lymphatic spread, i.e., perirectal, mesenteric and inguinal, were the most important and that hematogenous spread was secondary. Only two patients showed spread of the disease outside the confines of the pelvis or inguinal areas. One of these metastasized to the liver, which probably occurred through the portal venous system. A microscopic section (Figure II) demonstrates vessels obliterated by tumor in this patient. MacLean, et al[13] recently reviewed all reported instances of hepatic metastases and found a total of 24 patients. A rare instance of metastasis in our series was to the supraclavicular nodes.

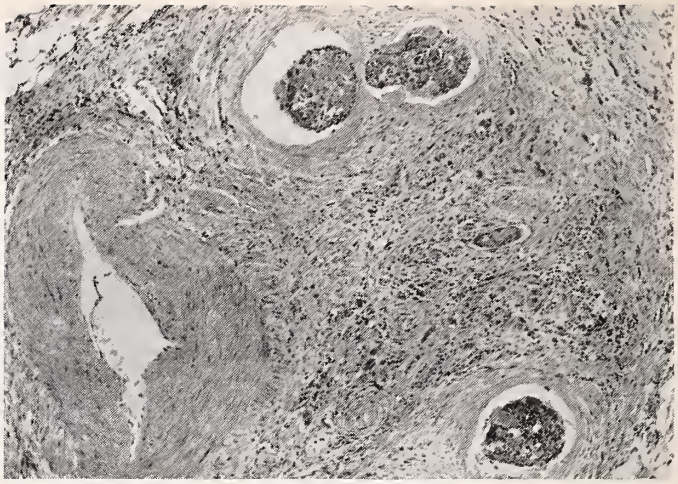

FIGURE II
Microscopic section of epidermoid carcinoma of the anal canal with vessel invasion. Magnified 114X.

In our 26 determinate patients, 17 showed metastatic lymphatic (15 patients) or hematogenous spread (2 patients). The lymphatic drainage areas of importance other than the nodes in close proximity to the tumor were (1) perirectal and mesenteric and (2) inguinal or femoral.

Since the iliac and hypogastric nodes are not routinely removed in the abdominoperineal procedure used at Hartford Hospital, no evaluation of this area of lymphatic drainage can be ascertained. A composite diagram of the sites of metastases proven by pathologic examination in the present series is shown in Figure III.

Results Of Treatment

Three of our early patients were treated solely by radiation, either by external source or radon seed implantation. Each of these cases developed complications such as stricture, fistula formation, or severe pruritis.

Eleven of our 26 consecutive patients survived five years (42%). Seven of the eleven survivors were treated by abdominoperineal resection. Three strictly perianal lesions were treated by wide local excision, and one was treated by biopsy and radon seed implant.

In an analysis of the 15 cases of non survivors, all of whom had anal canal lesions, seven had

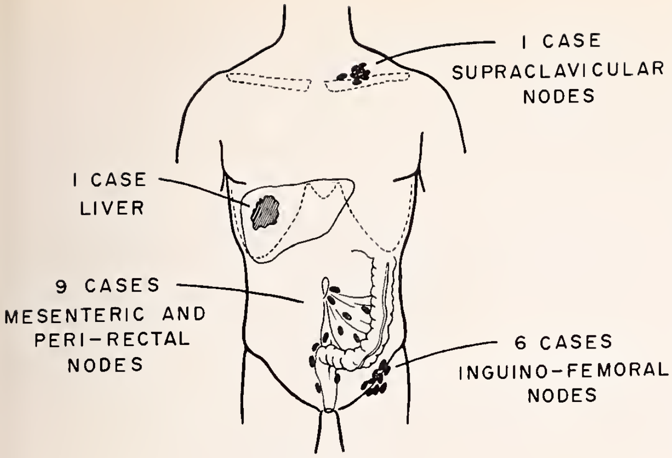

Figure III

Composite diagram of the sites of metastases from epidermoid carcinoma of the anal canal and perianal skin of 17 cases with metastases.

abdominoperineal resections, two had removal of the rectum with establishment of a colostomy, three were treated solely by radiation, and two had radiation followed by abdominoperineal resection. Three of the seven patients of non survivors in the abdominoperineal resection group had pathologically proven local recurrence with involvement of the urethra, bladder or vaginal septum. This could indicate inadequate excision of skin margins with the abdominoperineal resection.

Treatment

Because of the high incidence of pelvic and inguinal node involvement in our series (50%) and because there is considerable doubt among surgeons, radiologists and pathologists as to whether radiation can selectively penetrate the pelvis and destroy cancer in the perirectal or mesocolic nodes, it would seem that radical surgery would have the most to offer at the present time in the treatment of anal canal lesions. Three of our five-year survivors had positive perirectal or mesenteric nodes at the time of abdominoperineal resection and one five-year survivor had an abdominoperineal resection followed by metastases to the inguinal nodes subsequently treated by excision and external radiation. He has now survived 10 years since the diagnosis of inguinal node metastases.

All of the present patients who initially had or later developed inguinal node metastases (6 cases) had the tumor originate in the anal canal, involved the mucocutaneous junction and were not perianal. In contrast to this, Stearns[17] has reported perianal lesions with groin metastases.

If the lesion is strictly perianal and does not involve the anal verge or anocutaneous junction, a wide local excision can be performed. The local excision, however, should include sufficient marginal tissue from the anal canal and sufficient subcutaneous tissue so that the specimen can be adequately examined for local infiltration.

If there is any doubt concerning the anatomic location or infiltration of the tumor and to be absolutely sure about the skin margins and possible lymphatic spread, a radical approach, i.e., abdominoperineal resection with wide local excision of the skin and levator muscles, and high ligation of the inferior mesenteric vessels should be done. In females the posterior vaginal wall should be sacrificed. Buxton[5] has previously emphasized this point.

Summary And Conclusions

1. Twenty-six consecutive patients with epidermoid carcinoma of the anal canal and perianal skin followed five years at Hartford Hospital are presented.

2. Radical surgery, i.e., abdominoperineal resection with wide local excision of the skin and levator ani muscles and high ligation of the inferior mesenteric vessels, should be done in anal canal lesions. Perianal skin lesions can be treated by wide local excision or radiation, if the anocutaneous margin is not involved. Enough tissue should be removed from the anal canal for biopsy purposes in all perianal lesions.

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MEANING OF THE SCIENTIFIC REVOLUTION

It is not a simple question to answer why the scientific revolution occurred when it did. It started, as all serious historians would agree, in the Middle Ages and early Renaissance, and was very slow at first. No great culture has been free of curiosity and reflection, of contemplation and thought. "To know the causes of things" is something that serious men have always wanted, a quest that serious societies have sustained. No great culture has been free of inventive genius. If we think of the culture of Greece, and the following Hellenistic and Roman period, it is particularly puzzling that the scientific revolution did not occur then. The Greeks discovered something without which our contemporary world would not be what it is: standards of rigour, the idea of proof, the idea of logical necessity, the idea that one thing implies another. Without that, science is very nearly impossible, for unless there is a quasi-rigid structure of implication and necessity, then if something turns out not to be what one expected, one will have no way of finding out where the wrong point is: one has no way of correcting himself, of finding the error. But this is something that the Greeks had early in their history. They were curious and inventive; they did not experiment in the scale of modern days, but they did many experiments; they had as we have only recently learned to appreciate a very high degree of technical and technological sophistication. They could make very subtle and complicated instruments; and they did, though they did not write much about it. Possibly the Greeks did not make the scientific revolution because of some flaw in communication. They were a small society, and it may be that there were not quite enough people involved.

In a matter of history, we cannot assign a unique cause, precisely because the event itself is unique; you cannot test, to see if you have it right. I think that the best guess is that it took something that was not present in Chinese civilization, that was wholly absent in Indian civilization, and absent also from Greco-Roman civilization. It needed an idea of progress, not limited to better understanding for this idea the Greeks had. It took an idea of progress which has more to do with the human condition, which is well expressed by the second half of the famous Christian dichotomy—faith and works; the notion that the betterment of man's condition, his civility, had meaning; that we all had a responsibility to it, a duty to it, and to man. I think that it was when this basic idea of man's condition, which supplements the other worldly aspects of religion, was fortified and fructified between the 13th and 15th centuries by the re-discovery of the ancient world's scientists, philosophers, and mathematicians, that there was the beginning of the scientific age. By the 17th century there were a handful of men involved in improving human knowledge, or "useful knowledge" as the phrases went, so that new societies like the Royal Society and the Academy were formed, where people could talk to each other and bring to the prosecution of science that indispensable element of working together, of communication, of correcting the other fellow's errors and admiring the other fellow's skills, thus creating the first truly scientific communities.

—J. Robert Oppenheimer. "On Science and Culture." *Encounter,* October, 1962, p. 5.

Pseudoglaucoma

Henry L. Birge, M.D.

■ Pseudoglaucoma, defined as false, or deceptive, or deceitful glaucoma, with or without ocular damage, plays a larger role than is generally acknowledged in our handling of glaucoma.

Criteria For The Diagnosis Of Pseudoglaucoma

It is very difficult to know where one stands with the category of the pseudoglaucomas because we are discussing both the normal eye that behaves as though it had glaucoma, and the glaucomatous eye that behaves, at least for a time, as though it did not have glaucoma.

Cases may be seen in which there is marked glaucomatous cupping of the optic nerve, with extensive visual field loss, and normal or sub-normal ocular tension. Such cases may have a hereditary tendency. Fuchs (1911)[1] Deutsch (1961)[2] Sandvig (1961)[3] described them.

Pseudoglaucoma may also be found in an early stage, without visual impairment. It may resemble primary glaucoma, or narrow angle glaucoma. The difficulties and importance of the diagnosis of pseudoglaucoma will be emphasized. The increasing frequency with which pseudoglaucoma is mentioned or suggested in the literature reveal that several different mechanisms can bring about a state deceptively similar to glaucoma.

Each of the suspected causes of pseudoglaucoma will be mentioned and illustrative patient histories will be discussed in an attempt to improve the understanding of this confusing syndrome, and to show the necessary concern for the correct diagnosis. The diagnosis of pseudoglaucoma is as important as is the diagnosis of glaucoma.

Classification Of Pseudoglaucoma

1. Glaucoma without ocular hypertension
   “Low tension glaucoma”
   Inherited[1,2,3]
2. Glaucoma with systemic hypertension
3. Glaucoma with arterial hypotension[6]
4. Glaucoma with arteriosclerosis in various areas[6,7,8]
5. Glaucoma with hyposecretion of aqueous as)
   after epinephone—Diamox[9]
   “ epinephrine—miotics[25]
   “ circulatory arteration
   “ cyclodialysis[26]
   “ cyclodiathermy
6. Glaucoma with hypersecretion of aqueous
   as in antonmic nervous system overaction
   “ “ adrenals[14]
   thyrotropic exophthalmos[19,23]
   Mongolian idiots
7. Glaucoma with low scleral rigidity[18,22]
8. Glaucoma with high scleral rigidity[22]
9. Glaucoma with increased intra-ocular volume[22]
10. Glaucoma with decreased intra-ocular volume[22]
11. Glaucoma with false positive provocation tests[9]
12. Glaucoma with aberrant homeo static reflexes
13. Other forms of pseudoglaucoma[10,11]

The diagnosis of glaucoma, once made, is one of the most difficult to reverse. Even using all the complicated tools of the modern ophthalmologist, there remains a rather large number of cases in which there is an overlap of some of the findings on which glaucoma is diagnosed, with the findings in the normal eye. The percentage of overlapping findings is unknown at the present time. It is generally agreed that 2 per cent of the population over 40 years, in surveys for glaucoma will be positive. Yet, the percentage of false positives or pseudoglaucoma has not been agreed upon.

It seems logical to state that the earlier the diagnosis of glaucoma is attempted, the larger the ratio of pseudoglaucoma will be. We therefore should tighten the requirements for the diagnosis of glaucoma, rather than loosen them, if we are to reduce

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* *See Case Histories. Published in* Tr. AOS. *1962.*

* *Definition of Glaucoma* (Haik).[4]

Glaucoma may be defined as a disease in which the intraocular pressure is elevated to a degree which the eye cannot tolerate without damage to its structures. The increased pressure may be intermittent or constant. In the interpretation of this definition, it must be remembered that the intraocular pressure varies from individual to individual, as well as different times in the same individual. Furthermore, susceptibility to pressure damage also varies. Glaucomatous damage may therefore occur in eyes in which the pressure apears to be well within the so-called “normal” range.

(The diagnosis of glaucoma cannot be made, therefore, until *damage* occurs.)

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the number of pseudoglaucomas that are under treatment for glaucoma.

It would seem wise to put each new case of glaucoma through a system, or planned series of tests, to rule out pseudoglaucoma. Whether we use tonography, or applanation tonometry or combinations of tests to diagnose glaucoma, there are bound to be a percentage of cases in which only time alone will make the diagnosis between pseudoglaucoma and glaucoma. If we are to take advantage of "time" for the solution of this problem, we must withhold the diagnosis of glaucoma until there are progressive visual field losses indicative of glaucoma. Such defects may be found early using 1/1000 test objects. Caution again must be urged in using 1/1000 field tests to diagnose glaucoma.

The use of "time" in making the diagnosis of glaucoma is more important in view of the fact that a comparatively small percentage of practicing clinical ophthalmologists are as yet performing tonography or using applanation tonometry.

TONOMETRY

Pseudoglaucoma should be ruled out before each diagnosis of glaucoma is made. The zone of greatest confusion lies in the reading and interpretation of the ocular tension. I have found no cases in which the tonometer reading was reported to be over 42 mm. Hg., Schiotz, in which there was any question of the diagnosis of glaucoma.

Tension readings between 17 and 35 mm. Hg. represent the group in which the diagnosis must be scrutinized most carefully.

Every effort should be made to obtain the "baseline" tension. Nursing assistance in holding lid retractors is too little emphasized. In worried or nervous individuals the use of pentothal or barbiturate sedation should be emphasized. The diagnosis is important enough to recommend 24 hours bed rest in the hospital, in cases that require extreme sedation.

The care of the tonometer and its use should never be given over to a technician, or nurse.

If these stringent requirements are carried out by the ophthalmologist, it makes little difference which method of tonometry is used.

INTERPRETATION OF TONOMETRIC READINGS

The majority of tension readings should be performed as an office procedure. Tonography also is usually an office procedure, and because of the time and understanding required, must be performed by an expert, if it is to be dependable. Whether a 4 or 7 minute tonograph is used depends upon the judgment of the expert performing the graph.

The use of two Schiotz tonometers as well as the use of two weights on each eye, offer further safety measures.[15]

If the diagnosis of glaucoma is to be made at tensions over 22 mm. Hg., more attention is required to rule of the pseudoglaucomas. It can be agreed that the clinical diagnosis of glaucoma never depends upon 0.5 mm. Hg. variation in the tension reading.[17] The most frequent factors that confuse the diagnostician are factors involved with nervous tension in the patient, or faulty or too refined tension measurements. The first 11 classifications of pseudoglaucoma are among the least frequent, in my experience.

When the Schiotz tonometer alone is to be the basis of the diagnosis, several readings, over a period of "time" are important, in early cases of glaucoma, without definite field changes.

Multiple readings over several days are also important for the initial diagnosis of "low tension" glaucoma with field defects and optic nerve cupping.

When dependable tonography is available this offers a most reliable criteria for the diagnosis of True glaucoma and the separation of those cases representing pseudoglaucoma.

Reflexes[12] controlling both the outflow of aqueous and the inflow, have been studied by many workers. That these reflexes significantly affect the pressure reading of the normal eye has been shown by Armaly.[15] He recommends that low C values in tonography of the second eye be disregarded, and that the chief attention be given to low C values in the first tonogram, as a means of diagnosing pseudoglaucoma. While these regulatory processes are not fully understood in the normal eye, they are less well reported for glaucomatous eyes.

Tonography varies, with the same factors that cause variations in tonometry, and may also need to be repeated. It must be carried out in a tranquil atmosphere and away from the activity of a busy clinic.

It is too early to offer general comments on applanation tonometry in this country. The few men who have this tonometer available, the slow delivery of additional applanation devices, and the lack of experienced ophthalmologists or technicians, reserve the applanation tonometer for research, at this time.

The interpretation of accurate tonometric readings holds the key to the proper diagnosis of pseudoglaucoma, in most instances. If sufficient care is used in obtaining the readings with the Schiotz tonometer, or the tonograph and electronic tonometer, accuracy of the highest order will be obtained. To the accurate readings must be added sufficient time to study all aspects of the individual under consideration, and mature clinical judgment.

The diagnosis of pseudoglaucoma is the responsibility of the clinical ophthalmologist. The use of arbitrary didactic tension levels is no longer tenable for the proper diagnosis of glaucoma. Pseudoglaucoma of various types has been shown to exist between tension readings of 17 and 35 mm. of Hg.

Provocative Tests For Glaucoma

It might be well to emphasize the generally accepted rule that one high tension reading does not "make" the diagnosis of glaucoma.

This can be clearly stated by using a classification of glaucoma which, while it is in many clinicians minds, has not been used, namely:

I Pseudoglaucoma
II Prodromal glaucoma
III Glaucoma:—etc. then proceed with the (Haik) [4] classification as adopted by the Council for International Organizations of Medical Sciences, Canada, 1954. (Frolick) [16]

The interpretation of the results of provocative tests of glaucoma is subject to greater variation and consequent difficulty than is simple tonometry or tonography.[9]

Becker's interesting comments on provocative tests will assist in the diagnosis of pseudoglaucoma if properly used. He showed that many eyes with narrow angles occlude on pupillary dilation, but only a few showed a rise in pressure by tonometry. (An 8 mm. rise was considered diagnostic.) With tonography, a 25 per cent reduction in outflow facility was considered positive and found in 83 per cent of 48 eyes with angle closure capacity. The greater value of the more sensitive test (tonography) requires more judgment in its use. Both sides of the coin must be evaluated:—Glaucoma vs. Pseudoglaucoma.

In simple glaucoma the water drinking test was considered a valuable provocative manoever. Interestingly, only 30 per cent of proven glaucoma eyes showed a 8 mm. rise in tension (Schiotz) after water drinking. Tonography was more sensitive than tonometry in this group also, but Becker[9] was not willing to call all of the 90 per cent of such eyes that showed a Po/C over 100, true glaucoma. (pg. 129)

Becker and others[22, 23, 25] recommend that all eyes with intra-ocular pressure of more than 20 mm. Hg., or with facility of outflow of less than 0.20 be carefully evaluated for glaucoma. It seems a corallary that these cases require as careful evaluation for presudoglaucoma.

VISUAL FIELDS

The diagnosis of pseudoglaucoma can not be made from visual field studies alone. Cases have been shown with no visual field defects as well as with typical advanced glaucoma type defects.

Mention can well be made of several entities in which visual field defects resemble those found in pseudoglaucoma.

Retinoscheisis, meningiomata, arteriosclerosis of the choroid or of the vessels around the circle of Willis, and others, make it important for the diagnostician to check all field defects personally. Reports from technicians or assistants may be suggestive, but require verification. Here again "*time*" is an important adjunct to the correct diagnosis. Proper timing of examinations reveals the repeatability of the defect, whether or not progress is taking place, and may be made use of to establish a sound prognosis for the future.

OPHTHALMOSCOPY: GONIOSCOPY

Cupping of the optic disc may be caused by glaucoma, but the diagnosis of glaucoma depends upon associated findings. The diagnosis of pseudoglaucoma can not be made with the ophthalmoscope alone, nor with the gonioscope. Both of these examinations are an important part of the complete eye examination.

INCIDENCE

The incidence of pseudoglaucoma has yet to be determined. Variations in incidence are to be expected in different examiners experience. Pseudoglaucoma may occur in eyes with deep anterior chambers or with shallow anterior chambers. Pseudoglaucoma may exist for several years, and have true glaucoma develop. The diagnosis of pseudoglaucoma precludes any treatment other than observation, and this status is of immense benefit to the patient, especially patients who have unnecessarily been placed upon miotic therapy or more vigorous procedures.

HEREDITY

Pseudoglaucoma, of the low tension variety may be inherited.

The inheritance factor may also mislead the clinician. Three sisters all came to our office diagnosed as glaucoma, and under miotic therapy by three different ophthalmologists. Each physician gave undue importance to the history in other siblings. These high strung, 40 year old sisters all had ocular tension, repeatedly, of 20 mm. Hg. or under, without therapy, and Po/C ratios of 70 to 90 upon repeated tests over six months.

AGE FACTOR

In this series, the pseudoglaucoma diagnosis was made equally in the 3rd, 4th and 5th decade. In the younger patients, nervous tension was more of a factor, and in the older patients, arteriosclerosis was more important. No definite age factor can be described for pseudoglaucoma. One of our cases occurred in a 10 year old moron.

SEX

We found more women than men with the diagnosis of pseudoglaucoma.

PROOF OF THE DIAGNOSIS

In this series of cases,* diagnosed and under glaucoma treatment, who later were found to have normal tension without therapy over prolonged periods of observation proof is a matter of clinical judgment, and time.

Discussion Of Various Types Of Pseudoglaucoma

I. VARIATIONS IN SCLERAL RIGIDITY AND INTRA-OCULAR VOLUME RELATED TO PSEUDOGLAUCOMA

Pseudoglaucoma is a syndrome involving the interrelation of several factors, no more clearly shown than by the increasing realization that Friedenwald's coefficient of rigidity depends for some of its variations as much upon ocular volume as it does upon scleral rigidity. Hypothetically stated—given two eyes of differing initial volumes, with identical internal pressures, an equal tonometric load will indent the larger eye more than the smaller.

This principal of civil engineering was demonstrated experimentally by Phillips & Quick[13] and is similarly suggested by Goldman[20, 17] through his coefficient of distensibility. Sampson & Girard[22] demonstrated how corrected volume readings gave more constant scleral rigidity readings.

It is seen clinically when indentation tonometry is based upon average sized eyes, and the same scale and reading is used for larger eyes or smaller eyes than the average. The larger eyes give lower than usual tension readings, while the smaller eyes give higher than usual readings.

Until, (if ever) the applanation tonometer is as widely used as the Schiotz or Electric tonometers, the variations due to the coefficient of scleral rigidity, and intra-ocular volume, will be one of the major factors in the diagnosis of glaucoma. Applanation tonometry produces a very small change in volume (0.44 Cu. mm.)[10, 11, 17, 20] while impression tonometry and tonography may produce over 10 times the volume change (5.0 Cu. mm.) Goldmann (pg. 201).

In myopia it is to be noted that the larger eye has greater volume, often a thinner sclera, and often a flatter cornea. Sorsby[21] points out that many large eyes are not myopic, even though they have more volume, due to their size.

In buphthalmos, as the childs eye develops larger volume, the indentation tonometer should read a lower tension, although the actual tension may remain the same. Phillips and Quick[13] hypothesize that as the eye enlarges, it may develop better outflow channels, and also, because of the greater volume, may be able to "accommodate" greater pressure elevations than in its smaller state. In spite of these beneficial effects of ocular enlargement, early surgery appears to offer better long term results, in buphthalmos.

In small eyes, hyperopic usually, even in microphthalmos, the opposite effect upon the indentation tonometer is seen, and higher pressure readings are recorded, due to the smaller volume. Early surgery for glaucoma is to be carefully considered in these small eyes, and more reliability attributed to the visual field findings than to borderline tonometer readings.

Variations in ocular tension in cases of exophthalmos have been investigated by several authors and reviewed by Ytteborg[23] (1961). Both orbital tumors and thyrotropic exophthalmos[19] showed many cases with reduced scleral rigidity. Both the rigidity coefficient and the tension varied more as the exophthalmos increased.

Factors considered important in this situation were deformation of the posterior pole of the eye. The intraocular blood volume, the pressure in the recipient veins, partial oculomotor paralysis, and others. The complexity of the diagnosis of the scleral rigidity and its variations forms one of the difficult areas in which pseudoglaucoma is found.

II. LOW TENSION GLAUCOMA

Pseudoglaucoma of Autosomal Dominant Inheritance, defined as a condition of normal intra-ocular pressure with cupping of the disc and glaucomatous field changes, by Sandvig,[3] presents the typical syndrome of low tension glaucoma.

Sandvig suggests that the term *"low tension glaucoma"* should be reserved for cases showing impaired outflow facility or low scleral rigidity, while the term *"pseudogclaucoma"* should be used in the rest of the cases showing field defects, cupping of the discs and normal tension.

In the three families described there were 11 certain cases of pseudogclaucoma and seven probable. Some of the cases (5) had been described by Wium in 1948.

There were *no* cases of True glaucoma found in any member of these three families, over the years of observation.

Sandvig[3] quotes Becker[25] as believing that patients with normal intra-ocular pressure and glaucomatous field defects can be classified as having

1. Impaired outflow facility, spontaneous or from hypo secretion, as shown by atrophy of the ciliary processes, or

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* Published elsewhere. *Tr. AOS* 1962.

2. Low scleral rigidity;—such cases may have increased intra-ocular pressure but errors in measurement are due to low scleral rigidity.

Deutsch[2] reported two case histories in which progressive visual field loss typical of glaucoma occurred with no elevation of ocular tension and moderate cupping of the nerves. These cases had negative provocative tests for glaucoma. In both of these cases pilocarpine was used, but field defects progressed. The C value in both cases was less than 0.20.

These cases were correctly called "Low tension glaucoma," because of the progressive visual field loss. Deutsch felt that the vascular changes in the optic nerve probably explained these cases.

Fuchs[1] first in 1911 described a state of "relative glaucoma" due to "weakening" of the lamina cribrosa, which allowed even a normal intra-ocular pressure to cause field defects typical of glaucoma.

III. GLAUCOMA AND SYSTEMIC BLOOD PRESSURE VARIATIONS

McLean[5] in 1947 noted that cases of controlled glaucoma, when placed on serpasil or related drugs for the reduction of their excessive blood pressure, could show progressive visual loss when the blood pressure was maintained at reduced levels.

It is logical to suppose that a blood pressure of 300 mm. Hg. systolic could deliver enough blood and nutrition to an eye which was in a state of partially controlled glaucoma, with perhaps an ocular tension of 35 or 40 mm. Hg., and that under these conditions no optic nerve damage would occur, while the equilibrium lasted.

IV. OPHTHALMODYNAMOMETRY AND GLAUCOMA

The equilibrium between blood pressure and ocular pressure does not only show up in the hypertensive, it exists in normo-tensives and in hypotension, and must be kept in mind throughout the treatment of glaucoma.

The measurement of the ocular blood pressure by dynamometry in glaucoma has been recommended by Lobstein *et al.*[6] They followed some cases as long as nine years, and concluded that hypotension has an adverse effect on glaucomatous eyes, while hypertension acted to conserve visual integrity in a remarkable fashion.

The diagnosis of pseudoglaucoma must include knowledge of the systemic blood pressure, more specific than can be obtained from a survey of the retinal vessels. On the other hand, Simone[36] found no relation between the brachial blood pressure and the course of the glaucoma in 222 cases.

V. PSEUDOGLAUCOMA AND ARTERIOSCLEROSIS

Different grades of arteriosclerosis[7,8] occur in different areas of the body, and some of them produce visual loss indistinguishable from glaucoma. The most common of these is thought to be in the carotids at the chiasm and the next most likely area is in the choroid where sclerosis of varying degrees can be observed, even in the same eye, in different quandrants of the retina.

Pseudoglaucoma of this type is usually seen in people over 60 years of age, and many times miotic drugs are used in hopes of lowering the normal ocular tension so that the reduced nutrition supplied by the diseased vessels may go farther in preserving vision. Occasionally surgery is resorted to, but the results have not been encouraging in this age group even though tension in the eye has been reduced to below 10 mm. Hg.

The management of these elderly people with progressive visual field loss includes complete care, of the ocular tension, the sclerosing factors, diabetes together with observation of their systemic blood pressure.

Management Of Pseudoglaucoma

Pseudoglaucoma is seen to include factors of scleral rigidity, ocular volume, reduced out-flow facility and tonometric measurement.

The effect of arteriosclerosis, aging, blood pressure levels, stress, and inheritance are all to be given due consideration.

Just as the diagnosis of glaucoma requires damage[4] to the visual integrity, so does pseudoglaucoma. With problems suggestive of pseudoglaucoma, but without visual loss, a more proper diagnosis is Prodromal glaucoma.

Pseudoglaucoma is primarily to be managed as a medical problem. The use of miotics, anti-sclerosing routines, with care of the blood pressure levels, and necessary treatment of other conditions such as diabetes, are indicated.

The management of Prodromal glaucoma is one of watchful waiting, without producing anxiety on the part of the patient. Stress itself may initiate glaucoma when there are cooperative elements, either physiologic or psychologic.

The diagnostic dividing line between pseudoglaucoma and glaucoma has been shown to be indistinct, in many cases.

Summary

The Syndrome or Pseudoglaucoma, including as it does, both normal eyes and glaucomatous eyes, is most complicated. What is presently known has been discussed.

It does not seem to be referrable to any but the clinical ophthalmologist. "Time" is one of the important factors in the diagnosis;—not only the "time" the patient is observed, but also the time the clinician has been meeting the problems of glaucoma.

The many possible controversial ideas on Pseudoglaucoma deserve careful consideration, in view of the gravity of the diagnosis of glaucoma.

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A Guide To Foot-Care In Patients With Poor Arterial Circulation

Michael Hume, M.D.

■ Proper care of the feet by patients with peripheral arterial insufficiency is a joint responsibility of the doctor and his patient. Prevention of complications arising in the feet and toes is helped by educating the patient, but even the bare essentials of good foot care involves so many points that no patient could be expected to remember them unless put down in writing. Printed instructions in the form reported here have been used in the Outpatient Department of the Yale-New Haven Medical Center during the past two years. They are based on material previously published[1,2] and were revised by the sections of cardiovascular surgery, dermatology and metabolism of the Yale University School of Medicine, the Nursing Service of the Grace-New Haven Community Hospital, the Visiting Nurse Association of New Haven, and a podiatric consultant. The instructions are printed on both sides of a single page, and the patient is required to read them completely before leaving the Outpatient Department. Any questions about the instructions are answered. If the patient cannot read the form, a member of the family is asked to do so. When necessary, the Visiting Nurse Association is requested to review the matter in a home visit. These instructions are limited to the care of feet in the absence of the complications of arterial insufficiency. Acute ischemia, ulceration and other complications, of course, require special instructions appropriate to the situation.

From the Department of Surgery, Yale University School of Medicine.

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Valuable assistance in preparing these instructions was obtained from F. H. Epstein, M.D., P. K. Bondy, M.D., A. B. Lerner, M.D., M-L. Johnson, M.D., C. E. Falls, R.N., and I. Yale, D.S.C.

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A MEDICAL AND NURSING CARE GUIDE FOR THE CARE OF THE FEET OF PERSONS HAVING IMPAIRED ARTERIAL CIRCULATION

(Please read this carefully now, and ask any questions you may have of the doctor or nurse before you leave.)

1. Cleanliness

Truly your feet should be "as clean as your face!" Each night the feet should be bathed in lukewarm water using a mild soap. Test the water to be sure it is not too hot, using a bath thermometer (100-105°F.). If one is not available, test the water on the wrist. Dry feet by patting—not by hard rubbing. Avoid "sawing" the towel between the toes or pulling them forcibly apart, for this may cause a break in the skin. Dust on a small amount of talcum, brushing off the excess so that caking of the powder between the toes does not occur.

2. Dry Skin

If the skin is scaly or very dry, apply a small amount of lanolin. Rub this in well and do not leave an excess on the skin. Feet having any moisture on the skin do not need this treatment.

3. The Toenails

After the nails have been softened by bathing, using a good light, file them straight across with an emery board. Never cut nails down at the corners; this encourages the flesh to grow over the nail, giving rise to "ingrown" nails, pain and possibly infection. A knife should never be used on the toenails. If unable to care for the toenails ask a member of the family to help, or ask your physician to recommend a reliable foot specialist. Be certain to tell him of your poor circulation.

4. Fungus Infection

Dermatophytosis or "athlete's foot" is a nuisance when it involves normal feet and is dangerous when the circulation is poor. Signs of athlete's foot infection are softening of the skin between the toes, wetness, cracks, blisters or a tendency for the skin to shed when rubbed. Strong medicine to treat fungus infection is not good and many advertised "cures" may harm feet with poor circulation. A good solution is made by dissolving one five-grain tablet of potassium permanganate in three quarts of lukewarm water, and the feet soaked in this for ten minutes daily. This will stain the skin but this is harmless and temporary. To prevent a recurrence, use a foot powder such as Desenex and avoid stockings that cause excess sweating. The stockings may have to be changed twice a day. Your doctor will give you a prescription for potassium permanganate tablets. They are for external use only and should be stored in a safe place. Desenex foot powder can be obtained without a prescription.

5. Selection Of Shoes

Loosely fitting laced shoes with soft uppers and rigid shank are best, and new shoes should be chosen on the basis of this general type, and a good fit, rather than by appearance. Pointed shoes crowd the toes and should be avoided. A new pair of shoes should be worn on the first day for a half hour only in the evening and then for a longer period each successive evening. It is quite desirable to have two pair of shoes for every day use, to wear them on alternate days, and keep shoetrees in those not being worn. This will lessen the chance of developing calluses. Dry wet shoes on shoetrees, but do not put them near a heater. Wornout shoes with frayed liners or protruding nails should be repaired or thrown away.

6. Clothing

Dress properly for the weather, paying particular attention not to get the shoes or stockings wet. Rubbers or overshoes must be worn in wet or very cold weather. In the winter, plain wool socks should be worn and changed daily. When the weather is warm, cotton socks of medium weight may be worn, if wool or nylon causes sweating of the feet. Color dyes in stockings may irritate sensitive feet, plain white stockings are better. Do not wear garters that circle the leg. Women's stockings should be held up by a garter belt or girdle. At night, loose fitting woolen socks worn in bed protect the feet against rubbing on the sheets. The bed clothes should not be tucked in so tightly around the bottom of the bed that they press upon the toes.

7. Corns And Calluses

Proper fitting shoes and stockings will prevent the development of corns and calluses. Avoid medicated corn plasters which usually contain strong acids. Rather than trying to cut a callus, ask your physician to refer you to a reliable foot specialist. Advise him that you have impaired circulation.

8. Injuries

Whether it is a blister, an ingrown or split toenail, a cut from broken glass, a burn from a heating pad, a strong medicine like tincture of iodine, or frostbite,—any injury to a foot with poor circulation may cause trouble. It is your responsibility to prevent these accidents. The skin of the feet must never come in contact directly with anything which could cause a burn, cut or blister. Do not walk barefoot in the dark. Small injuries involving a break in the skin should be cleaned thoroughly with soap and covered with a sterile gauze dressing. It is dangerous to think they will "heal in a few days." Consult your physician before continuing normal activity whenever there is an injury or signs of redness or swelling.

9. Exercise

Moderate exercise is not harmful if the other recommendations noted above are observed.

10. Tobacco

Smoking causes a decrease in the volume of flow of blood to the extremities and a decrease in the skin temperature of the fingers and toes. Clinical observations made upon patients having impaired arterial circulation leaves no doubt that tobacco is harmful.

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COUNCIL MEETING SUMMARY OF ACTIONS

November 21, 1963

I. Attendance

Present in addition to the Chairman, Dr. Martin, were: Drs. Pitock, Gilman, Cullen, Goldberg, Hess, Weise, Sr., Scully, Wilson, O'Connor, Bradley, Grendon, Grant, Phillips, Shepard, Dean, Seigle, Gevalt, Egan, Abbot, Caplan, Spitz. Also present: Mrs. Lindquist and Mr. Burch. Absent were: Drs. Gardner, Davis, Hughes, Weber, Jr., Ciccarelli, Hastings, Medbury, and Richards.

II. Routine Business

Approval Of Minutes

It was VOTED to approve the minutes of the meeting of October 23, 1963, as printed and distributed.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members.

William A. Tanner, Danielson (WCMA)
Samuel D. Schupack, New Britain (HCMA)

Exemption From Dues

It was VOTED to exempt the following members from payment of CSMS annual dues as follows and for the reasons indicated:

Hubbard Lynch, Fairfield (FCMA)—1963—Physical Disability. (Dr. Lynch will become a Life Member on 1/1/64.)

Lester Q. Stewart, West Hartford (HCMA)—Duration of his Physical Disability beginning with the year 1963.

Committee Resignations, Appointments

Committee On Third Party Payments

It was VOTED to accept, with regret, the resignation of Arnold H. Janzen, Hartford, as Chairman of this Committee, and that he be requested to remain a member of the Committee. It was further VOTED to appoint Max Caplan, Meriden, as Chairman of the Committee for the remainder of the current year.

Committee On State Blood Bank

It was VOTED to accept the resignation of Sawyer E. Medbury, Willimantic, as a member of this Committee. Dr. Medbury informed the Council that he is transferring his practice to Springfield, Massachusetts.

Committee On Accident Prevention

It was VOTED to accept the resignation of Allan J. Ryan, Meriden, as Chairman of this Committee and as Chairman of the Socio-Environmental Medicine Division, as of December 1, 1963. Dr. Ryan has accepted the Chairmanship of a Committee of the American College of Sports Medicine and the U. S. Olympic Committee. It was further VOTED to appoint Malcolm S. Beinfield, Westport, as Chairman of the Committee on Accident Prevention for the remainder of the current year and that J. Wister Meigs, New Haven, be appointed as Chairman of the Socio-Environmental Medicine Division. Dr. Meigs is Chairman of the Committee on Occupational Health.

Cancer Coordinating Committee

After review of the resolution on cigarette smoking which was adopted by the FCMA on October 2, 1963, approved by the CCC, and the alternate resolution submitted by the Committee on Public Health, it was VOTED to adopt the latter, as follows:

WHEREAS, the Connecticut State Medical Society represents the medical profession of the State of Connecticut; and

WHEREAS, this Society is aware of its responsibility to the citizens of the State of Connecticut; and

WHEREAS, the preponderance of evidence indicates that cigarette smoking is strongly implicated in the genesis of lung cancer, chronic bronchitis, and emphysema; and

WHEREAS, there is a strong statistical association between cigarette smoking and illness and death from coronary artery disease; therefore be it

RESOLVED, that the Connecticut State Medical Society go on record as advocating the giving up of cigarette smoking by those already habituated; and be it further

RESOLVED, that the Connecticut State Medical Society further go on record as advocating that the youth of our state be encouraged not to acquire the tobacco habit for health reasons; and be it further

RESOLVED, that the Connecticut State Medical Society officially endorse programs of teaching these dangers to health from smoking to the grade and high school level youth of our state, and that a copy of this resolution be sent to the Commissioner of Education for the State of Connecticut.

It was further VOTED that the FCMA be informed that its resolution on cigarette smoking was accepted as information and that a resolution which the Council believes is in consonance with the FCMA version will be presented to the House of Delegates on December 11.

Cancer Coordinating Committee

It was VOTED to accept, with minor revision, the following three recommendations submitted by the Committee:

1. Inform all members that the Society favors yearly Pap smears on all women over 25 years of age.
2. Record the Society as favoring demonstration projects which reveal the effectiveness of exfoliative cytology in the early detection of cancer.
3. The Society to suggest to hospital staff chiefs, that it favors a Pap smear on all female admissions who are over 25 years of age and who have not had a Pap smear examination within the year.

This information is to be transmitted to the membership of CSMS through CONNECTCUT MEDICINE.

Committee On Public Relations

It was VOTED that the report prepared by this Committee on the request of the AMA Department of Medicine and Religion (that the Society and its component associations appoint committees to undertake liaison studies and educational programs jointly with clergies of the major faiths) be referred to the county associations.

It was VOTED to accept as information the report of the Committee on the possibility of obtaining free TV and radio time on WNHC, New Haven.

It was VOTED that the "Proposal for a Communications Conference with Allied Groups" be referred back to the Committee for further study and more details as to type of program and audience, and to inform the Committee that the Council approves of the general idea of such a conference.

Mr. James Burch, Public Relations Director, presented a detailed report on the "Connecticut Physicians' Communications Program" which outlined a functional classification of communications activities. It was VOTED to accept this report as information.

Committee On Public Health

It was VOTED to approve the "Vaccination Assistance Project Grant" which would be administered by the State Department of Health. The main purpose of this project is to immunize children under five years of age against poliomyelitis, diphtheria, tetanus and pertussis. This is part of a nation-wide program to raise the immunization levels of such children against these four diseases.

Date Of Next Meeting

December 18th was tentatively set as the date for the next meeting.

III. Old, New And Special Business

Total Legal Responsibility Of Surgeon

Dr. Jacques Green, North Haven, filed with the Council a report on his study of the question as to the total legal responsibility of a surgeon for the negligence or malpractice of other persons in an operating room, especially the anesthetist. It was VOTED that an opinion rendered by the Society's legal counsel and Dr. Green's report, excerpts of which follow, be accepted as information.

"In accordance with your (the Council's) request, I have consulted with . . . legal counsel (and) received their written opinion 'as to the total responsibility of a surgeon for the negligence or malpractice in the operating room, primarily the anesthetist.'

(Legal counsel states) that a qualified anesthetist is not under the control of, or responsible to, the surgeon. Counsel also states that, although as a matter of legal theory the surgeon should therefore not be responsible (for the acts of the anesthetist), nevertheless the application of this principle to a specific instance must depend on its own particular facts.

(In view of counsel's finding) that Connecticut courts have not had occasion to consider and rule on this question, (it is not possible) to give assurance that the surgeon is free from all possible liability for the actions of the anesthetist."

The 1964 Budget

Printed copies of the proposed budget, as prepared by a sub-committee, had been distributed to all members of the Council prior to the meeting and Isadore S. Goldberg, Chairman of the subcommittee reported in detail on the various items.

The subcommittee reported that projecting the Journal deficit of $10,000-$15,000 in 1964 and anticipating further sizeable legal costs, and noting that dues exemptions have practically cancelled out any increase in dues paying members, the 1964 budget as submitted was a very tight one and that it was more than likely that the Society would have to use surplus funds again by the end of 1964. No provision was made by the subcommittee for legal costs, because it was an unknown factor.

It was VOTED that an item of $10,000.00 be inserted into the 1964 Budget for anticipated legal expenses and it was further VOTED that the 1964 annual dues be set at $45.00 and to recommend approval of the Budget by the House of Delegates on December 11, 1963. It was further VOTED that the Treasurer in presenting the 1964 Budget to the House of Delegates put special emphasis on the general considerations of his report.

Connecticut Medical Service

The Chairman read to the Council excerpts from the brief prepared by the Society's legal counsel. The single copy of the brief is available at the Society's office.

Report On Investments

A detailed report on the investment program of the Society's general fund, prepared by the Investment Counselor, was accepted as information.

Student Members

It was VOTED to elect 17 medical students to Student Membership in the Society.

Ad Hoc Committee On Resolution Number Two

Dr. Bradley, Chairman, presented a detailed report with recommendations on the resolution adopted by the House of Delegates on December 8, 1962, "Increasing the Availability of 'Service Benefits' Prepayment Plans." It was VOTED to adopt the report and recommendations of the committee and they will be transmitted to the Semi-Annual Meeting of the House of Delegates on December 11, 1963. Following are the recommendations contained in the report:

1. That the Connecticut State Medical Society adhere to its original 1948 objectives and current policies regarding guaranteed doctor-subsidized medical services for low-income groups and individuals, and that the Society continue to offer its support and guidance to any plan or plans featuring service benefits with which the Society has a written agreement that recognizes the Society as having a permanent and at least equal voice in the establishment of the professional and public policies of any such plan or plans.

2. That, as long as the Society continues to sponsor a single prepayment agency, it refrain from taking active steps to increase the availability of service benefits prepayment plans, either through non-profit or private sources.

3. That if and when circumstances or evidence confront the Society which indicate that a need has been created for increasing the availability of service benefits prepayment plans, the Society promptly undertake to develop such a plan or plans in conformance with the pertinent objectives and policies laid down by the House of Delegates.

4. That the Council and the House of Delegates consider, in separate action, the advisability of requesting that the Ad Hoc Committee on Resolution No. 2 utilize its study, thought, and experience to formulate a plan which would provide appropriate prepayment methods for the medical care of the people of Connecticut.

Norman J. Barker, a member of the Ad Hoc Committee mailed in a dissenting minority report to the Chairman of the Council. This was also presented to the Council.

N.B.: *The foregoing is a summary of the proceeding and actions of the Council on November 21, 1963. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

E.E.N.T. Specialist—Age 64 years, desires associated assistant, clinic work, locum tenens, etc. Certified by Board of Otolaryngology. Has Connecticut license.

UROLOGIST interested in association or partnership. Age 34. Available June 1964. Connecticut license.

PLACEMENT OPPORTUNITIES

FAIRFIELD COUNTY. For Sale—ten year General Practice, fast growing community. Price includes home with attached equipped office. Centrally located.

PEDIATRICIANS. Part time temporary for State Crippled Children Clinics, Norwich and Windham, monthly and Hartford Office two to four days per month.

State of Connecticut desires to fill a position for a physician in a State Training School and Hospital.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN ST., NEW HAVEN.

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ACCIDENT AND HEALTH PLAN

In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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STATEMENT OF THE CONNECTICUT STATE MEDICAL SOCIETY

RE: HR 3920, 88th Congress—"Hospital Insurance Act Of 1963" House Committee On Ways And Means

November 21, 1963

Mr. Chairman and Members of the Committee:

I am Dr. William R. Richards of New Haven, Connecticut, a private practitioner of medicine in that city for fourteen years and, since 1959, executive officer of the Connecticut State Medical Society. I have been authorized by the Society, a voluntary association of more than 3500 physician members, to present testimony at this hearing which will reflect the views of the Society and the vast majority of Connecticut's doctors toward HR 3920 and similar legislative proposals.

During the 87th Congress, the American Medical Association presented to the Committee on Ways and Means a statement of some 100 pages which evaluated in depth the purposes, philosophy and provisions of HR 4222, the immediate predecessor of the Bill now being heard. At that time, we in Connecticut found that the point-by-point critique presented by the AMA demonstrated clearly and conclusively that HR 4222 was a poor piece of legislation from almost every standpoint—its unpredictable cost, its built-in regulation of medical practice and professional judgment and, particularly, the false premise that such a program was needed. We find now that this new Bill—HR 3920—is subject to the same criticism, to the same extent, and for essentially the same reasons.

Overlooking for the moment the many objectionable provisions of the current King-Anderson offering, it is our wish today to emphasize what we believe to be the primary faults of these so-called "medicare" plans; *i.e.,* that they propose to needlessly initiate radical changes in the eminently successful American system of patient care, and that they propose to do this while turning a deaf ear and a blind eye to the attributes of our system which have made it operate so well for so long a time.

We doctors are constantly working toward an ever-higher quality of medical services, because we believe the quality of such services is the paramount consideration. We also favor the unlimited expansion of sound, *voluntary* programs for assisting all our people in paying for their personal health care. In HR 3920, however, we find little or nothing which would promote the realization of these twin goals and, indeed, find much that would tend to prevent it. In short, we contend that "social insurance" in medicine would be a sorry answer—if any answer at all—to such unmet needs in medical care and its financing as may still exist in the United States today.

It is to a factual evaluation of these "unmet needs" among the aged in Connecticut that we wish to limit our testimony on HR 3920 at this hearing. It is to several unfounded premises in the "Findings and Declaration of Purpose" of HR 3920 that we desire to address our arguments today.

In Connecticut, What Are The Facts About Private Insurance?

Examining the opening words of HR 3920, we read as follows: "The Congress hereby finds that . . . (2) Most of them (aged individuals) are not able to qualify for and to afford private insurance adequately protecting them against such (hospital and related health care) costs."

In Connecticut, every publicly known fact disproves this as a finding to be made by the Congress. Excluding from considerations some 15,000 permanently invalided aged who are being well cared for in state-operated institutions, and about the same number of indigent aged whose hospital care is furnished under the Old Age Assistance program, fully 85-90 per cent of the remaining 215,000 people over 65 have the same hospital insurance protection right now that is held by their children and grandchildren. Connecticut Blue Cross alone covers 154,000 of them (72 per cent) and commercial carriers have enrolled at least 80,000 others—figures which indicate that quite a number are electing to carry more than one type of policy. It is entirely unjustified, therefore, for anyone who is openminded to find that "most of them" cannot qualify for and afford this kind of private health insurance. The facts prove exactly the opposite to be the case.

As to the adequacy of such protection for the aged, a recent impartial survey in Connecticut was reported on by Mr. Thomas F. Walsh in *The Hartford Courant* for Sunday, October 21, 1962. His study showed that "those on Blue Cross had *most* of their room and board and *all* of their other services taken care of. Another (group), on commercial insurance plans, ran an average of from 70-80 per cent of their bill covered (by their policies)." In addition, it is of more than passing significance that this same survey found only 14 per cent among the over-65 group studied who did not have third party coverage and, in keeping with many other surveys, that no other segment of the population (including the "uncovered" 14 per cent) pays its hospital bills as fully and as promptly as do older people.

Touching on one of the major "related health care costs" referred to in the preamble to HR 3920, let us consider the nursing home situation in Connecticut. There are approximately 10,000 nursing home beds in our State (excluding state-operated chronic disease facilities), and these beds are occupied about equally between patients whose care is paid for through private means and those whose care is tax-supported. Among the latter group are some 5,000 former Old Age Assistance beneficiaries who have been transferred by the Department of Welfare to the Kerr-Mills roles. Among the former are a great many who are benefitting from enrollment in major medical programs such as the Connecticut 65 Plan which, alone, has paid out over $520,000 to convalescent hospitals during the 24 months of its operation. Now it may be argued, hypothetically, that there are some people at home who might be better off in one of these institutions or, less hypothetically, that quite a number of those now in residence are receiving custodial care which is only remotely medical, but the point we wish to stress here is that the entire group of over-65's in true need of nursing home attention at any given time is undoubtedly less than five per cent of the total and that, between voluntary private insurance and existing tax-supported programs, there is a mechanism available right now in Connecticut to assure nursing homes of being paid for their services to patients under a doctor's care.

It may be said, also, that the proven ability of the Nutmeg State's older people to fend for themselves in health matters is not limited to carrying protection against institutional costs. It is a matter of record that nearly the same number (about 200,000 or 85 per cent) subscribe as well to plans covering physicians' services. A single agency, Connecticut Medical Service (Blue Shield) has offered continuous open enrollment since 1959 and now has close to 130,000 members over age sixty-five, and commercial carriers furnish doctor-care coverage to better than 75,000 others.

Beyond basic insurance, upwards of 60,000 of Connecticut's older residents protect themselves against larger health costs under voluntary major medical plans.

Worthy of special mention, we feel, is the Connecticut 65 Plan—a joint pilot enterprise of 32 insurance companies which began operations 24 months ago. On the basis of experience, the Plan is presently seeking permission to make certain adjustments in its premium structure, and this has prompted local proponents of compulsory Social Security medicine for the aged to label this worthy program a "failure." We disagree completely. Connecticut 65 and the other major medical plans are paying out millions of dollars in benefits each year, and each million dollars from these sources represents a matching million which will *not* have to be taken out of Connecticut workingmen's pay envelopes (through King-Anderson) and withdrawn from our business and industrial communities.

In the light of these facts, then, we contend that the Congress could not possibly "find," in Connecticut, what the preamble of HR 3920 asks it to about private health insurance for the aged.

The Kerr-Mills Program In Connecticut

The Connecticut State Medical Society gave wholehearted support to enactment of the Kerr-Mills Law by the Congress in 1960, and to its implementation in our State by the 1961 General Assembly. Since its effective date of operation, April 15, 1962, Connecticut's MAA program of comprehensive and almost unlimited medical coverage has been available to all "near needy" residents who qualify.

At the 1963 session of our legislature, and with further support from our Society, amendments to P.L. 578 (our Kerr-Mills statute) were made which liberalized the eligibility criteria to include over-65's whose individual income is less than $1,800 per year (plus $150 for health insurance) or, for a married couple, less than $2,700 per year (plus $250 for health insurance), and which eliminated a $100 "deductible" requirement from the original law.

At the present time, there are approximately 7,000 people being carried as MAA clients. However, some 4,000 of these are former Old Age Assistance clients (completely indigent) who have been transferred on paper to the MAA roles in order to take advantage of the greater Federal matching funds under the MAA section of the Kerr-Mills Law. It is our judgment that this "juggling of the accounts," however financially advantageous to the State, tends to becloud the true picture of the need and effectiveness of MAA for the "near needy" and offers a clearcut reason for the Congress to permit a separate state agency to administer the MAA program.

From these figures, it can be seen that after nineteen months of operation, the Connecticut MAA program is benefitting not many more than 2,000 bonafide, *new* "medically indigent" persons. Now, some will argue that this demonstrates that Kerr-Mills is "not doing the job," inasmuch as so relatively few of the State's 245,000 aged are receiving these tax-supported health services. However, if one recalls that the truly indigent were already being taken care of, and that fully 85-90 per cent of the rest of our aged population is enrolled under private hospital and doctor-care insurance plans, then it is not surprising to find that such a small number appear to require financial help under MAA.

It may well be that, at both state and Federal levels, the provisions of the Kerr-Mills Law will need amending from time to time as experience indicates. But when one considers that for *strictly* MAA operation in Connecticut only $9 million of general taxes is required (State's share $4.5 million) yearly, it is our conviction that guaranteed protection of older people against possible pauperism as a result of illness can be managed quite economically, Contrast this modest cost, if you will, with that of the King-Anderson proposal which, as a beginning, would take $25 million or more in additional Social Security taxes out of the 'State annually (HEW estimate). If there is really any "pennies-a-day" aspect to any program of tax-supported financing of health services, it would certainly appear to apply more legitimately to the Kerr-Mills approach than to the Administration's proposal.

In summary, then, it is the opinion of the Connecticut State Medical Society that the size of the "near needy" or "medically indigent" segment of our aged population is small, and that the in-being operation and future potential of Connecticut's Kerr-Mills comprehensive program will provide sufficient protection for all those who demonstrate reasonable need for medical financial assistance, whether such need is total or only supplemental. Certainly the experience in our State does not at all bear out another "finding" in HR 3920 that "many . . . are accordingly forced to apply for private or public aid . . . ," nor do we expect it ever will.

Conclusion

On behalf of the Connecticut State Medical Society and its 3,500 physician members, I thank the Chairman and Members of the House Committee on Ways and Means for this opportunity to present testimony opposing the enactment of HR 3920, the so-called "Hospital Insurance Act of 1963." Although we are convinced that the Bill contains provision after provision which violate every principle of good medical practice and high quality of patient care, we have attempted to present the Committee only with facts on the medical and health insurance status of the aged in our State, and on the need for and operation of our Kerr-Mills program. In consideration of our testimony, we are most hopeful that a majority of the Committee members will agree with us that the Congressional "Findings" which HR 3920 calls for are largely unwarranted and will vote, at the appropriate time, *not* to file a favorable report on this Bill with the House of Representatives.

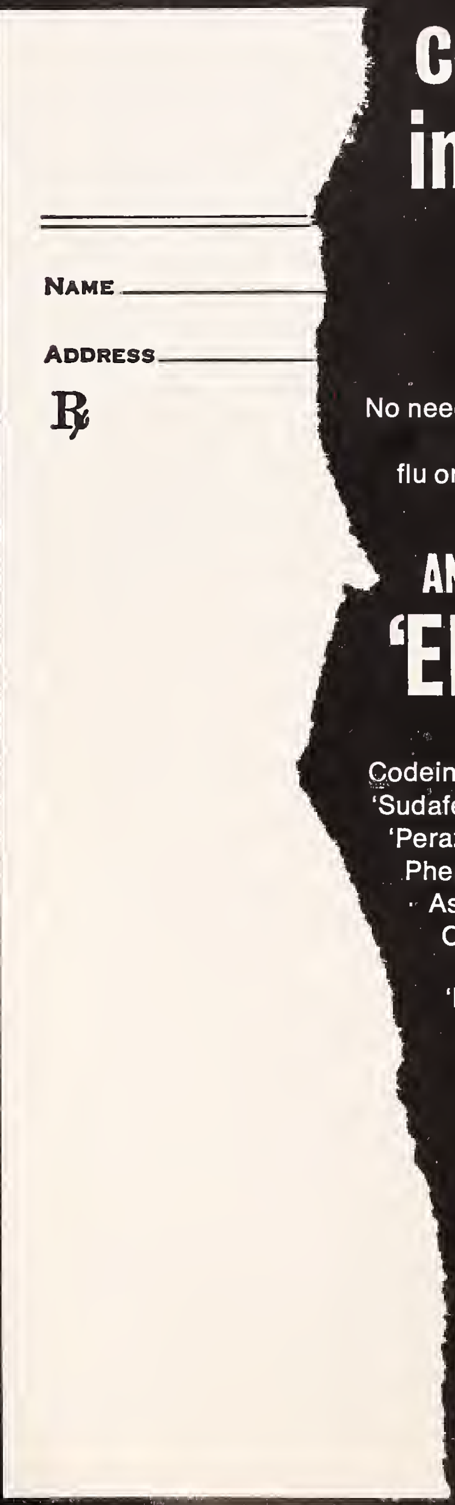
IMPORTANT — PLEASE NOTE

At the Council Meeting on November 21, 1963, the following recommendations of the Cancer Coordinating Committee were accepted:

"1. Inform all members that the Society favors yearly Pap Smears on all women over 25 years of age.

2. Record the Society as favoring demonstration projections which reveal the effectiveness of exfoliative cytology in the early detection of cancer.

3. The Society to suggest to hospital staff chiefs, that it favors a Pap smear on all female admissions who are over 25 years of age and who have not had a Pap smear examination within the year."



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SUMMARY OF ACTIONS
HOUSE OF DELEGATES — SEMI-ANNUAL MEETING
December 11, 1963

Reports Of Officers And Others

Reports were presented to the House by:

Officers: Morris P. Pitock, President; Ralph L. Gilman, President-Elect; Orvan W. Hess, Secretary; James R. Cullen, AMA Delegate; Norman H. Gardner, AMA Delegate.

Others: Stevens J. Martin, Chairman of the Council; William R. Richards, General Manager.

Those reports which were submitted in writing will be published in Connecticut Medicine.

Old Business

AMENDMENT TO THE BYLAWS

On a proposed amendment concerning "Membership," introduced and tabled at the meeting of April 30, 1963, it was voted to refer the proposed amendment back to the Council for further study and report by the Council's Subcommittee to Study and Revise the Bylaws.

REPORT ON RESOLUTION NO. 2, HOUSE OF DELEGATES, DECEMBER 4, 1962

Acting on the Report of the Council re: "Increasing the Availability of 'Service Benefits' Prepayment Plans":

(1) It was voted to accept the Report of the Council which made three recommendations as follows:

A. That the Connecticut State Medical Society adhere to its original 1948 objectives and current policies regarding guaranteed doctor-subsidized medical services for low-income groups and individuals, and that the Society continue to offer its support and guidance to any plan or plans featuring "Service Benefits" with which the Society has a written agreement that recognizes the Society as having a permanent and at least equal voice in the establishment of the professional and public policies of any such plan or plans.

B. That as long as the Society continues to sponsor a single prepayment agency, it refrain from taking active steps to increase the availability of "Service Benefits" prepayment plans, either through non-profit or private sources.

C. That if and when circumstances or evidence confront the Society which indicate that a need has been created for increasing the availability of "Service Benefits" prepayment plans, the Society undertake to develop such a plan or plans in conformance with the pertinent policies and objectives laid down by the House of Delegates.

(2) In a separate action, it was voted:

That the Council, through its Ad Hoc Committee, utilize the study, thought and experience of the Committee (which led to the preparation of this Report) to formulate a plan which would provide "appropriate prepayment methods for the medical care of the people of Connecticut."

A motion to refer the Report back to the Council for further study and report was defeated by a vote of 65-33.

New Business

BUDGET AND FIXING OF DUES FOR 1964

It was voted to accept the Budget for 1964, and the fixing of annual membership dues at $45, as recommended by the Council. The increase in dues was found to be necessary for two principal reasons as follows: (a) An anticipated deficit of $10,000-$15,000 in the operation of the Journal; (b) Anticipated and unanticipated legal costs of present and future projects.

REQUEST OF SECTION ON EENT

As recommended by the Council, it was voted to permit the present Section on EENT, by vote of its members, to dissolve and form two groups which will be known, respectively, as the Section on Ophthalmology and the section on Otorhinolaryngology.

RESOLUTION ON CIGARETTE SMOKING

As recommended by the Committee on Public Health, it was voted to adopt a resolution on cigarette smoking as follows:

"WHEREAS: The Connecticut State Medical Society represents the medical profession in the State of Connecticut, and

WHEREAS: The Society is aware of its responsibility to the citizens of the State of Connecticut, and

WHEREAS: The preponderance of evidence indicates that cigarette smoking is strongly implicated in the genesis of lung cancer, chronic bronchitis, and emphysema, and

WHEREAS: There is strong statistical association between cigarette smoking and illness and death from coronary artery disease, therefore be it

RESOLVED: That the Connecticut State Medical Society go on record as advocating the giving up of cigarette smoking by those already habituated, and be it further

RESOLVED: That the Connecticut State Medical Society also go on record as advocating that the youth of the State be encouraged not to acquire the tobacco habit, for health reasons, and be it further

RESOLVED: That the Connecticut State Medical Society officially endorse programs of teaching about these dangers to health from smoking to the grade and high school level youth of the State, and that a copy of this resolution be sent to the Commissioner of Education for the State of Connecticut."

INTERIM CHANGES IN DIVISIONAL BOARD AND MEMBERSHIP COMMITTEE

It was voted to approve a printed list of such changes, as submitted by the Council.

PROPOSED AMENDMENT TO THE BYLAWS

It was voted to receive a proposed amendment concerning the censorship function of the Council, presented by the Board of Directors of the Hartford County Medical Association, and to table the proposal for action at the next meeting of the House of Delegates, as required under the Bylaws of the Society.

REQUEST FOR GUIDANCE—CHAIRMAN OF THE COUNCIL

In response to a request for guidance by the House of Delegates, presented in his report by the Chairman of the Council, it was voted to adopt the following motion (introduced from the floor):

LEGAL ACTION RE CORPORATE PRACTICE OF MEDICINE

"IT IS MOVED: That the House of Delegates of the Connecticut State Medical Society, duly assembled in its semi-annual meeting on December 11, 1963 at Norwich, does hereby authorize the Council of the CSMS to undertake appropriate legal action, if the same be or become necessary, for the purpose of causing the termination of payments of money to hospitals by Connecticut Blue Cross (The Connecticut Hospital Service, Inc.) for services rendered to Blue Cross subscribers by physician-employees of said hospitals."

RESOLUTION ON FLOURIDATION

As presented in a report of the Committee on Public Health, it was voted to adopt a resolution on the fluoridation of communal water supplies as follows:

"WHEREAS: On April 27, 1953, the Connecticut State Medical Society's House of Delegates adopted the following Resolution:

> Resolved: That the House of Delegates of the Connecticut State Medical Society be recorded as favoring the flouridation of communal water supplies under regulations as may be established by the State Department of Health. and

WHEREAS: The Committee on Public Health has reviewed studies of the beneficial effects of flouridation in preventing tooth decay and the absence of any deleterious effect to health among 600,000 residents of this state now drinking water with fluoride controlled to provide a dilution of one part per million, therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm its action of 1953 favoring the fluoridation of communal water supplies under regulation of the State Department of Health."

Adjournment

Following adjournment, members and guests of the House of Delegates enjoyed a social hour graciously provided by their host, the New London County Medical Association.

REPORT OF THE CHAIRMAN OF THE COUNCIL

Mr. Speaker, Mr. President, Members
of the House and Guests:

Seven meetings of the Council have been held since the last session of the House of Delegates on April 30, 1963. A tremendous amount of routine and special business has been discussed and transacted during this period. In keeping with the Council's action of January 24th of this year, all Delegates have regularly received complete copies of the minutes of each meeting and therefore I do not propose to review at this time any but those matters upon which I feel special emphasis should be placed.

1. At the organizational meeting of the Council on May 9th, it was my great privilege to be elected Chairman of that body for 1963-64. Having some personal knowledge of the outstanding accomplishments of my recent predecessors in this office—Dr. Tom Feeney and Dr. Ralph Gilman—and also of the many trials and tribulations they faced, I can assure you that I have not undertaken the assignment lightly and that I have welcomed the cooperation and support extended to me by all members of the Council and members of the Society's office staff. If, as I suppose sometimes is bound to happen, the House or the general membership does not always

look with complete sympathy and favor on every action taken by the Council, I can only say to you—without reservation—that no decision is reached without full discussion or without following democratic and parliamentary procedure.

2. For nearly a year now, the Council has been attempting to grapple with a problem which is commonly referred to as "the corporate practice of medicine"—particularly in relation to hospitals. Following receipt of a rather broad and comprehensive legal evaluation of the question from Attorney Edward L. Marcus of New Haven last Spring, the Council turned over the difficult ask of "separating the wheat from the chaff" in this matter to a Subcommittee headed by Dr. David A. Grendon, Councilor from Litchfield County. At the present time, Dr. Grendon and his associates have determined to put aside the more general aspects of this whole subject and are pursuing a single one of its many facets—the Outpatient Rider currently being sold by Connecticut Blue Cross. This rider, as many of you know, is making payment for certain physicians' services to hospitals. It is the opinion of the Committee that a hospital service corporation is not authorized to make such payments under existing statutes. At the last Council meeting, Dr. Grendon reported that all avenues of reasonable negotiation between the parties concerned with this question are being explored and that a joint meeting of our representatives and Blue Cross spokesmen would be held shortly with the State Insurance Commissioner. The Committee is being advised constantly by legal counsel, and has been empowered to move ahead in this matter up to the point of taking overt legal action. On September 19, the Council voted to refer to the House of Delegates for approval any plan of action which would involve formal litigation, but, at the time this report is being written, I know of no specific plan of this nature which is ready for consideration by the House today. It occurs to me, however, that in keeping with its action last April on the CMS controversy, the House might authorize the Council to act to institute legal proceedings in this matter if it was determined to be "necessary." I would appreciate receiving guidance from the House on this question.

3. Operating under the new Bylaws of the Society which became effective on May 2, 1962, the Council has twice acted as the Board of Censors of the Society in hearing and ruling on appeals from disciplinary decisions of component associations. Under the able leadership of its first chairman, Dr. Ellwood C. Weise, Sr., and his successor, Dr. Michael R. Scully, the Council's Committee on Preliminary Study of Censorship Questions acted with distinction in preparing reports on the two cases heard, being assisted in its work by legal counsel. In one instance, the Council ruled contrary to the county decision and its rulings have been complied with. In the other, the Council sustained the decision of county component and so notified the lay plaintiff and physician defendant. At its last meeting, the Council was informed that the Hartford County Association's Board of Directors will introduce a proposed amendment to the Bylaws which would, in effect, limit the Council's censorship function to determining if the records of the county hearing made available to it are "material and sufficient to support the findings which the component association reached."

4. Dr. Franklin M. Foote, State Commissioner of Health, requested the Council to consider appointing an advisory committee to assist him in resolving questions concerned with "staff organization within the hospital to provide adequate control of the quality of various clinical services." The Council voted on May 29th to approve his request. Appointment of this Advisory Committee has been set up on a standby basis so that, should the Commissioner have a specific question on which he seeks advice or assistance, the Chairman and General Manager will designate committee members on the basis of the geographic location and type of practice appropriate to the circumstances, and will regularly include at least one member of the CSMS Committee on Hospitals. Since taking this action, I am pleased to report that the Council has received no request from Dr. Foote to furnish such an Advisory Committee.

5. Received too late to be presented to the House of Delegates at its last meeting, the Council reviewed on June 27 the 1962-63 annual report of the Advisory Committee to the Commissioners of Welfare, Finance and Control. Pursuant to this review, the Chairman wrote to the Commissioner of Welfare to inform him of certain opinions of the Council as follows:

a. That at all times, in all situations possible, patients eligible to receive MAA (Kerr-Mills) assistance should be taken care of by private physicians and be classified as private patients. Any patient who is taken care of on "ward service" at a community hospital should be placed in this category only because of his own free choice.

b. That MAA payments for anesthesiology services by a physician should be made to the physician performing the service. It is recognized that the MAA payment schedule is based on 75 per cent of the payment schedule of the CMS Preferred Contract, but it is the opinion of the Council that MAA need not be bound by CMS policy with respect to anesthesia benefits.

c. That MAA payments for physicians' services of all kinds (including radiation therapy, radio-active isotopes, etc.) should be made to physicians, wherever performed, and that payments to hospitals for physicians' services should not be authorized under MAA policy. This opinion applies equally to all care rendered by private physicians in hospital emergency rooms.

Receiving a somewhat less than satisfactory written reply from the Commissioner, and recalling the informational benefits which had accrued to the Society from an in-person meeting with Mr. Shapiro last year on the operation of the Medical Assistance for the Aged (Kerr-Mills) program, it was voted to ask the same Ad Hoc Committee to arrange another meeting with Welfare Department representatives for the purposes of: (a) reviewing the MAA program's over-all performance since April of 1962, (b) of discussing with them further the opinions of the Council which I have just referred to, and (c) the necessity for continuing to transfer whole groups of former Old Age Assistance beneficiaries to the MAA roles. I am informed that such a meeting is to be held on December 17th. We will await with interest the report of Dr. Weise and his Committee.

6. On April 30, 1962, the House of Delegates adopted a resolution which directed the Council to undertake two projects. The first of these was to "institute a realistic appraisal of hospital costs and accounting procedures." I am pleased to inform you that the Committee on Hospitals, under the able chairmanship of Dr. Leo Trifari, has undertaken this assignment for the Council and, after adequate preparation, held a most instructive seminar on this subject on November 20. It is my understanding that the Committee plans to utilize the information obtained at the seminar to pursue this appraisal and file a report on hospital costs and accounting procedures with the Council in time to permit its transmittal to the House of Delegates at the Spring meeting. The second portion of the resolution concerned the Society's "urging the State Insurance Commissioner to set a positive limit of payment by insurance companies, for hospital and medical services, of no more than 100 per cent of costs . . ." The Council has referred this matter to the Committee on Third Party Payments for study, but as yet no report has been forthcoming.

7. In September, the General Manager notified the Chairman in writing that his initial five-year contract with the Society would expire on May 1, 1964 and that, in accordance with the terms of the agreement, he was informing the Council of his desire to renew the contract. A Subcommittee of Drs. Pitock, Hess, Egan and Martin was appointed to study and report on this request. The Chairman is pleased to inform the House that, on October 23, the Council voted to offer the General Manager a second five-year agreement, starting on May 1st of next year, and that the General Manager accepted the offer with thanks.

8. For some time, the Council has been considering ways and means through which the Society could improve its effectiveness as a scientific organization, increase the efficiency of its administration, and modernize its system of internal and external communications and public relations. An Ad Hoc Committee was appointed by the Council a year ago September for this purpose. At the Council meetings of October 23rd and November 21st, it was voted to accept the report and recommendations of the Committee. As a consequence, in the next few months it is hoped that steps will be taken to accomplish such things as (a) To establish a Committee on Committees, which will review the operation of our numerous committee groups and divisions and attempt to make constructive suggestions to expedite their work; (b) to have the General Manager's office compile more comprehensive and continuing biographical records of our members; (c) to permit the Editor of *Connecticut Medicine* to gain assistance up to four Associate Editors of his choosing; and (d) to strengthen the public relations activities of the Society. Dr. Hess and the officers and others who served with his Committee are to be commended for their efforts in making this study.

9. The Medicare Contract, which covers the dependents of military personnel, was approved for 1963-64. While it is alleged that this contract is periodically "negotiated" with the Defense Department, it is disappointing to know that none of the contract changes proposed by our Medicare Committee and the Committee on Third Party Payments were approved by the government officials.

10. The 1964 Annual Meeting of the Society will be held at the Statler-Hilton Hotel in Hartford on April 28, 29 and 30. It is felt that the experience with the Hartford site has been most pleasant in the past two years. The Board of Governors of the New Haven County Association has been most gracious in passing up New Haven's turn to act as host for the Scientific Assembly next Spring.

11. With further reference to the Annual Meeting, Dr. Morris P. Pitock, our President and a Delegate to the Medical Society of the State of New York, Dr. E. Tremain Bradley, Councilor from Fairfield and Delegate to the New Jersey State

Medical Society, and Dr. Howard K. Ente, a Delegate to the New Hampshire Medical Society, have all filed detailed reports with the Council on their attendance at meetings of those several sister organizations. They brought to our attention the manner in which out-of-state representatives were received during those annual sessions. As a consequence of their somewhat "mixed notices" on the more social aspects of their respective receptions, the Chairman has followed a directive of the Council and appointed Drs. Pitock, Seigle, Wilson, Bradley and Richards as a committee to study and to make recommendations in regard to the matter of planning suitable welcoming, hospitality and entertainment procedures to be followed by the Society in acting as host to visiting delegates and other distinguished guests at our Annual Meetings.

12. Beyond the request of the Chairman that the House give the Council direction on the question of possibly instituting legal action with respect to the corporate practice of medicine, you have in your Delegate's agenda booklet several matters for action presented to you by the Council. Just for the record, I will enumerate these as follows:

(a) The Council's Report to the House of Delegates on Resolution No. 2, adopted by the House on December 4, 1962. Please correct this date in your copies. In error, the date is listed as *December 8, 1962.*

(b) The request of the EENT Section that it be allowed, by vote of its members, to dissolve and thereafter form separate Sections on Ophthalmology and on Otorhinolaryngology.

(c) The resolution on Cigarette Smoking, submitted by our Committee on Public Health, which has been adopted by the Council and is presented to the House of Delegates.

(d) The proposed amendment to the Bylaws on "Membership."

(e) The confirmation of interim changes in boards and committees as listed.

(f) The 1964 Budget and the fixing of dues for next year.

13. Concerning Connecticut Medical Service: Having received the support of the House "in its determination to defend the rights of all qualified members of the Society to be nominated by the Council to serve as representativs of the medical profession on the Board of Directors of CMS, Inc.," and pursuant to the directive of the House to "initiate appropriate legal action, if necessary, to compel the Corporators of CMS, Inc. to seat as CMS Directors the three (1963) nominees of the Council (who 'failed of election')," the Council reviewed the entire controversy with representatives of the Board at a liaison meting held in May. Since the CMS spokesmen declined to offer any explanation whatever as to the nature of the unacceptability of the three nominees in question, and since it was made clear that under no circumstances would the three rejected nominees be voted in as Directors, the Council *did* find it necessary to initiate legal action to attempt to achieve the objectives laid down by the House last April. The case was heard before the Superior Court of the State of Connecticut in New Haven on September 17, 18 and 19. Briefs and counter-briefs have since been filed by the attorneys for both sides, and the decision of the Court is expected to be handed down late this month or in early January. In essence, the position of the Society is that there is, and always has been, an implied agreement between the two agencies that the naming of the physician members of the Corporation is the prerogative of the Medical Society; that their so-called "election" as Directors is merely a ceremony; that, in fact, Drs. Davis, Caplan and Ente became members of the Corporation upon nomination by the Council; and that, in amending the CMS Bylaws on June 6, 1963, the incumbent and illegally constituted corporate members and directors deprived the Society of any meaningful voice in the operation of CMS as a medical service corporation under its sponsorship. The position taken by CMS, on the other hand, is that there is not, and never was, any agreement which gave the Society the right to name the physician members of the Corporation, that the nominations of the Council are considered by the Corporators to be only suggestions, to be elected or not as the incumbent Corporators see fit; and that the sponsorship of the Society, while desirable to have, is in no sense necessary to the management of the Plan in the public interest. As I have said, a court decision in this matter is expected in the near future. I believe the House is hopeful—as the Council is—that the Society's position will be sustained. If it is not, I can assure you that the Delegates will be given full opportunity to arrive at whatever further decisions it may be necessary to make in this deplorable situation.

Conclusion

14. Once again, I want to acknowledge the capacity for hard work and the dedication to discharging their duties which have been displayed by the members of the Council. The Chairman is grateful to the members for their support and advice, and is also most appreciative of the efforts of Mrs. Josephine P. Lindquist and Dr. William R. Richards to furnish him with timely and wholehearted cooperation.

Respectfully submitted,
STEVENS J. MARTIN, M.D.
Chairman of the Council.

who were the “untreatables”?

From their inception with cortisone, to the present-day variants of the steroid molecule, the corticosteroids have presented a therapeutic paradox. The beneficial action against inflammation and allergy as well as several undesirable metabolic effects are all, apparently, the results of the same basic physiologic action.[1]

Some of these associated metabolic reactions made it risky or otherwise undesirable to treat with steroids large numbers of patients in various categories who would otherwise have benefited from such management. These "untreatables" were overweight, had cardiac disease, hypertension, or pulmonary fibrosis associated with congestive heart failure. Also in this category were those patients whose emotional symptoms were aggravated by earlier steroids.

But the advent of ARISTOCORT® Triamcinolone in 1958—the result of biochemical and pharmacologic research which successfully stripped away many important undesirable hormonal effects from the primary anti-inflammatory action—dramatically changed this picture. This steroid did not overstimulate the appetite, or cause the excessive weight gain induced by other steroids;[2-7] it proved to have one of the best records of any steroid for *not* causing edema, or salt-and-water retention;[2,3,7-10] and the incidence of undesirable euphoria with this agent was remarkably low.[2,4,5,9,10] What is most significant is that these benefits have stood the test of more than 5 years of widespread use. And, of course, the avoidance of these distressing hormonal effects benefited *all* patients requiring steroids, not just those in the special categories, as demonstrated by wide clinical use.

Side Effects. Since it may, under some circumstances, produce any of the unwanted effects common to all cortisone-like drugs, discrimination should always be exercised in administering ARISTOCORT® Triamcinolone. Any of the Cushingoid effects are possible, as are purpura, G.I. ulceration, increased intracranial pressure and subcapsular cataract. Corticosteroids generally may mask outward signs of bacterial or viral infections. Catabolic effects to watch for include muscle weakness and osteoporosis. Weight loss may occur early in treatment but is usually self-limiting.

Contraindications. While the only absolute contraindications are tuberculosis and herpes simplex, there are some relative contraindications (peptic ulcer, glomerulonephritis, myasthenia gravis, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, psychic disturbance, pregnancy, infection) to weigh against expected benefits.

While no steroid can *cure* a susceptible disorder, many patients who would otherwise be confined in a state of invalidism have, on ARISTOCORT® Triamcinolone, been able to pursue active, useful lives.

References: 1. Levine, R.: Rationale for the Use of Adrenal Steroids, Paper presented at Annual Convention, Medical Society of the State of New York, New York, May 13-17, 1963. 2. Hollander, J. L.: Clinical Use of Dexamethasone. *JAMA 172*:306 (Jan. 23) 1960. 3. Boland, E. W.: Chemically Modified Adrenocortical Steroids. *JAMA 174*:835 (Oct. 15) 1960. 4. McGavack, T. H.: The Newer Synthetic Adrenocortical Steroids in Therapy. *Nebraska Med. J. 44*:377 (Aug.) 1959. 5. Freyberg, R. H.: Berntsen, C. A., Jr., and Hellman, L.: Further Experiences with Δ1, 9 Alpha Fluoro, 16 Alpha Hydroxyhydrocortisone (Triamcinolone) in Treatment of Patients with Rheumatoid Arthritis. *Arthritis Rheum. 1*:215 (June) 1958. 6. Cahn, M. M. and Levy, E. J.: Triamcinolone in the Treatment of Dermatoses. *Amer. Practit. 10*:993 (June) 1959. 7. AMA Council on Drugs: New and Nonofficial Drugs. *JAMA 169*:255 (Jan. 17) 1959. 8. McGavack, T. H.; Kao, K.-Y. T.; Leake, D. A.; Bauer, H. G., and Berger, H. E.: Clinical Experiences with Triamcinolone in Elderly Men. *Amer. J. Med. Sci. 236*:720 (Dec.) 1958. 9. Fernandez-Herlihy, L.: III. Use and Abuse of Corticosteroid Therapy—The Structure and Biologic Activity of the Corticosteroid Hormones and ACTH, *Med. Clin. N. Amer. 44*:509 (Mar.) 1960. 10. McGavack, T. H.: Triamcinolone: A Potent Anti-inflammatory Sodium Excreting Adrenosteroid. *Clin. Med. 6*:997 (June) 1959.

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REPORT OF THE PRESIDENT

Mr. Speaker, Dr. Martin, Dr. Gilman, Members of the Council, Members of the House of Delegates and Guests:

Since the Annual Meeting of our Society, held on April 30, 1963, there have been some rather unusual developments. You are probably familiar with most of these developments through their being reported in Connecticut Medicine. Nevertheless, I feel their significance needs pointing up.

We have a new Chairman of the Council in the able person of Stevens J. Martin of Hartford County. He always looks surprised at how efficiently the Council is functioning under his chairmanship, but we knew it would be that way when we elected him. As for myself, I find my association with the Council one of the most satisfying experiences of my life. It speaks well for the democratic process that our County Medical Associations so consistently select men of such outstanding ability to represent them in the Council.

I could speak volumes on my association with our General Manager, but I would only embarrass him. In my ignorance, I used to think he had a pretty cushy job—with regular nine-to-five hours, good pay, and security. Having spent the last seven months in close association with him on Society business, I have long since been disabused of that notion. We are fortunate, indeed, to claim as our own one of such ability, dedication and loyalty as Bill Richards.

One word of advice. Let us be sure to hang on to Mrs. Josephine Lindquist. She is billed as Assistant to the General Manager. But some day, some medical association in need of a superior executive secretary will try to steal her away from us and, in my judgment, we couldn't afford to lose her.

Now about the events of the last seven months: The most outstanding of these events has been the court action taken by the Society against CMS. When CMS rejected our nominees to the Board of Directors, we considered this action contrary to the Bylaws under which we were operating as the Plan's sponsor. When they requested us to submit five or six nominees, from which they could choose three, we rejected that request. To have acquiesced would have been tantamount to yielding up our right to name the CMS physician Corporators and to choose our own representatives on the Board of Directors. When the incumbent CMS Board changed the Bylaws of CMS, we considered that action to be illegal. We were therefore forced to initiate court action to obtain clarification of our rights in our conflict with CMS. You will be further informed by our Council Chairman on this subject, so I will leave the details to him. I do wish to emphasize, however, the urgent necessity for having sound legal advice and for maintaining good written records in all business transactions involving the Society. The General Manager has stressed to the Council the part played by our past neglect in these matters in the court action now pending.

While we are on the subject of legal counsel, there have been several occasions on which such counsel was needed; i.e., in the question of the responsibility of the psychiatrist in his professional co-operation with a psychologist and, again, in the question of the total responsibility of the attending surgeon for all aspects of care of his hospitalized patient. In an age when the doctor is forced to practice with one eye on the statutes, it is apparent that legal guidance is essential to our Society's function. It is a costly function, as you will note in reviewing the budget, but it could be costlier to omit this budgetary item.

I can also report that the House of Delegates' resolution regarding the cost of hospital care is now "work in progress" by two of our committees, the Committee on Hospitals and the Committee on Third Party Payments.

The Council's subcommittee on the corporate practice of medicine has worked assiduously under the able chairmanship of Dr. David A. Grendon. In the near future, the Council will make recommendations to the House of Delegates on this problem.

The Ad Hoc Committee, appointed by the Council, has concluded its studies on Resolution 2 and is reporting its findings and recommendations to you under "Old Business" on the agenda.

Your Council has undertaken a study of the Society's committee and staff structure, and a committee, chaired by Dr. Hess, has filed a definitive report. This is an effort to improve the efficiency of committee work and of the numerous duties assigned to the office staff.

As must be obvious, our Society is a living organism, and, as is characteristic of all living things, it is in constant change. As our problems become more complex, we must evolve new methods for coping with them. I have referred to many of these problems in my President's Page in the Journal. In my appearances at the county association meetings, one of the notable problems seems to be the paucity of member participation in association affairs, and it is interesting to observe the manner in which this problem is being approached. Elements of compulsion are creeping into our county associations' bylaws. Time alone can tell whether this method is good or bad. Certainly compulsion in greater or lesser degree is a condition of our

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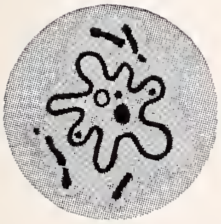

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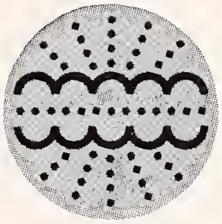

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Research in the Service of Medicine **SEARLE** daily lives, whether in our hospital functions or the legal or economic aspects of private practice. Nor do these compulsions apply only to the medical profession. But insofar as they do apply to us, we must retain our resiliency and adaptability to changing conditions. Only by remaining alert and flexible can we continue to exert a meaningful influence on our times in the field in which we excel —American Medicine.

Morris P. Pitock, M.D.
President

REPORT OF THE GENERAL MANAGER

Mr. Speaker, Mr. President, Members of the House and Guests:

On November 21st, it was my privilege to appear in person before the House Committee on Ways and Means in the nation's capitol and, on behalf of the Society, to present to the Committee a statement in opposition to the enactment of the current version of the King-Anderson Bill, the so-called "Hospital Insurance Act of 1963." The full text of our statement will be published in the January issue of Connecticut Medicine, but, in brief, I will characterize it for you as testimony containing a maximum of factual information and an absolute minimum of emotion and tilting at windmills.

In essence, the statement placed emphasis on the point of view that the primary faults of all these "medicare" plans is that "they propose to *needlessly* initiate radical changes in the eminently successful American system of patient care," and that their sponsors make this proposal while "turning a deaf ear and a blind eye to the very attributes of our voluntary system which have made it operate so well for so long a time."

As evidence to sustain our criticism of this "deaf ear and blind eye" approach, and to back up our contention that King-Anderson legislation is not needed, we offered detailed health insurance facts about the aged in Connecticut which make entirely unwarranted any finding by the Congress (quoting from HR 3920) that "most of the aged are not able to qualify for and to afford private insurance adequately protecting them" against hospital costs. We also presented facts about our Connecticut Kerr-Mills program which make it equally unwarranted for the Congress to find (quoting from the Bill again) that "many aged persons . . . are forced to apply for private or public aid." I am pleased to report that quite a number of people I talked to in the hearing room, including several who admitted favor for Social Security medicine, told me they found the information we submitted to be convincing as well as enlightening.

Having listened carefully to the exhaustive testimony which was admirably presented by the American Medical Association, and to the uniformly excellent reports filed by a dozen or so of our sister state societies and by other agencies, I can concur heartily with Dr. Annis' conclusion that the combined weight of all this factual evidence probably "made a far greater impact on the members of the (House Ways and Means) Committee, friend and foe alike, than at any time in the history of this long and bitter conflict." I say this—and not as a biased optimist—because while the proponents of compulsory medical care were singing pretty much the same old song of poverty and disease that has been their stock-in-trade since the time of the Murray-Wagner-Dingel proposal, we, its opponents, were documenting an almost unbelievable record of progress and achievement in medical care and medical care financing under a free system. This time, most of us avoided reference to "socialized medicine"—although we still contend that that would be a guaranteed consequence of passage of the King-Anderson Bill. Instead, we applied ourselves to the task of presenting arguments which we could substantiate with actual proof. This "proof," I might say, is something American medicine didn't have too much of a few years ago—we just didn't know what the facts were—but today it is available to us in ample and increasing supply. This is so not only in high-income states like our own, but also in most political subdivisions throughout the nation.

Nowadays, we hear a great deal about how Congress seems to be "dragging its feet" on certain major legislation, and how something ought to be done to "streamline" its present *modus operandi*. However, I think the majority of onlookers who sat through the long hours of hearings on this medicare bill came away with a deep conviction that many responsible representatives of the people are acting wisely in not allowing undue haste to make immeasurable waste of the personal freedom and economic substance of those who have elected them to office. These matters are complex and, as a first-time, firsthand observer of a Congressional committee in action, I can certainly vouch for the fact that a great deal of time is needed to furnish open-minded members of the committee with all the information they consider essential to making sound legislative decisions. By those legislators with closed minds and pre-determined political points of view, on the other hand, I imagine that such lengthy seekings for the truth are held to be both boring and inexpedient. Fortunately, it appeared to me, the latter group was in a numerical minority on the Ways and Means Committee.

It was also my assessment of the proceedings that some of the more prominent of the witnesses who were granted unlimited time (we were allowed only seven minutes) brought out little of pertinence to the matter-at-hand and, in several cases, fell apart at the seams rather badly when their testimony was subjected to questioning. As one example, take the plight of HEW Secretary Celebrezze who, as leadoff man for the Administration, laid great stress on the "pennies-a-day" cost to the working man of the King-Anderson scheme. Imagine his embarrassment when, a little later on, Chairman Mills elicited from one of the Secretary's staff of experts that the Department, without knowing it, has been underestimating the anticipated outlay of funds for hospital benefits by 100 per cent or more right along, and that the increase in Social Security taxes which Mr. Celebrezze had presented to the Committee as fact would therefore have to be doubled if even a pretense of solvency were to be assured for the program.

Or take the situation in which the Secretary of Agriculture, Mr. Freeman, found himself when he finished reading *his* prepared statement. On being questioned by Representative Tom Curtis of Missouri, the Secretary admitted that he had served recently with a Federal Commission which made a study of the aged—he said, in fact, that it had been his "great privilege' to take an active part in the preparation of the Commission's report—but then proved himself able to recall almost *none* of the facts, figures and conclusions which had been derived from the study. Further, when asked what he would "guess" the report showed on a number of key points, even if he didn't *know,* Mr. Freeman's replies turned out to be wrong about 90 per cent of the time when checked against a printed copy of the document offered in evidence by his questioner. At the close of his testimony, Chairman Mills thanked the Secretary for presenting his views on medicare to the Committee and observed that perhaps he, too, had learned something from his appearance. When Mr. Freeman replied: "I certainly have, Mr. Chairman!", to no one's surprise the dignified decorum of the hearing collapsed completely and a hearty and prolonged laugh was enjoyed by all.

So, as I have said, I think it can be claimed fairly that if what the Committee wanted to get were facts about the health care of the aged, it received a great deal more of them from those who testified in opposition to HR 3920 than from those who testified for it, including the officials I have just mentioned and several other prominent political figures.

As all of you well know, a terrible tragedy befell the nation on November 22nd, even while the hearings were still in progress. I am sure there is not a one of us who does not deplore the violence that resulted in the President's assassination, or who does not feel personal grief that such a fine young American has been lost to his country and to his family. However, I for one cannot share the opinion now being broadcast from so many sources that those of us who hold a conservative political philosophy were in some way responsible for the enactment of that senseless murder. In the practice of medicine, certainly, there is no place for hatred or like emotions and I do not believe that any physician would ever harbor such feelings against anyone—no matter how strongly he disagreed with another person's views.

Yet that these base emotions do flourish in some quarters today, no one can deny—and I have with me tangible proof that this is so. Upon returning home from Washington on that fateful Friday, my good wife reluctantly presented me with this postcard which I show you now. Addressed to: "Dr.? William R. Richards, Veterinary," the card has affixed to it a New Haven newsclip which reports on my attendance at the hearings and conveys to me the following message: "When America turns communist, it'll be because of anti-public bastards like you. The reason you're rich is because you robbed the poor people during all your career." As you might expect, the card is not signed.

Now, speaking facetiously, I suppose I ought to dismiss this anonymous harassment by trying to say something funny about it—like claiming that I deeply resent having anyone call me "anti-public." Speaking seriously, however, I suggest that the poor, twisted soul who put together this message of hate was addressing it not just to me but to every physician, everywhere. It is an affront to each of us, but how does one go about making a reply to those who choose to hide from the public view? Speaking for myself, I intend to disregard these groundless attacks upon my character and integrity and to continue to speak out as a free citizen of a free country in defense of what I believe in. In my judgment, none of us can do less in our efforts to preserve our constitutional liberties. We owe it to ourselves to do this because we are members of an honorable profession and, especially, because we have the great good fortune to be Americans.

Respectfully submitted,
William R. Richards, M.D.
General Manager

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Mental Health

The Suicide Prevention Program of the A.M.A. as outlined by Mrs. Robert L. Garrard, National Mental Health chairman, has been discussed by the state committee. The film "The Cry For Help" has been secured for a showing in Hartford County by that county chairman, Mrs. Paul Graffagnino. All County presidents, Mental Health chairmen and the members of their committees have been invited to see this film on Tuesday, January 14, 1964 at 10:00 A.M. in the auditorium of the Institute of Living at 400 Washington Street, Hartford. Dr. Raymond Veeder, clinical director of the institute will discuss the film subsequently and conduct a question and answer period. It is hoped that other counties will also use this film.

Scholarships Awarded

The Memorial Scholarship Fund of Hartford County has this year awarded ten scholarships totalling $3,600 to eight boys and two girls attending medical schools. Fifty students have received aid totalling over $34,000 since the beginning of this fund in 1948.

Middlesex County has announced the awarding of a scholarship to Linda Carter who is a medical technology student in training at Middlesex Memorial Hospital.

Other counties have announced plans to make further awards this year.

Auxiliary Notes

AMA-ERF projects are now in full swing in all of the counties. Several counties have announced successful sales of playing cards and note paper.

Hartford County is planning the annual Medi-Capers dance for the benefit of the Scholarship Fund to be held in late January.

Middlesex County reports that Clinton has become interested in their Health Careers program.

Fairfield held a Health Careers Day program for the twelve hospitals in the Bridgeport area in December and will hold a similar program January 16, 1964 in Greenwich for the high schools in that area.

A "Hobby and Food Tasting Fair" in New Haven County realized about $350.00 for their scholarship fund.

At the December meeting of the Board of the State Auxiliary the unexpended balance of the 1962-63 budget was transferred to the savings account.

The Legislative Committee announced the cessation of hearings on the King-Anderson Bill in Washington, which hearings will be resumed at a later date to be announced by Chairman Mills.

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

Around The State

Litchfield County Medical Association

The Litchfield County Medical Association will hold a scientific meeting Tuesday, February 11th at the Charlotte Hungerford Hospital, Torrington at 8:00 P.M.

The speaker will be Dr. Lee W. Henderson, University of Pennsylvania Hospital.

Dr. Henderson's topic of discussion will be "Peritoneal Dialysis."

1964 MEETINGS

January 20-23—Postgraduate course sponsored by the Department of Medicine, Hahnemann Medical College and Hospital. "Cardiovascular Drug Therapy" – Marriott Motor Hotel, Philadelphia.

March 19 – 180th Annual Meeting of the New Haven County Medical Association will be held at Waverly Inn, Cheshire, Conn. Business Meeting scheduled for 2:30 P.M.

April 28-30—Annual Meeting Connecticut State Medical Society, to be held at Statler-Hilton Hotel, Hartford.

May 25-27—Annual Meeting American Thoracic Society Medical Section of the National Tuberculosis Association to be held in New York City.

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

CONNECTICUT MEDICAL POLITICAL ACTION COMMITTEE

announces . . .

A SYMPOSIUM ON POLITICS '64

Sunday, January 19, 1964

Waverly Inn, Cheshire

1:00 P.M. Registration for Physicians and Wives

This symposium is planned by COMPAC to provide an opportunity for physicians and their wives to meet in person prominent and well informed political leaders.

Highlight of the meeting will be an address by James D. Weaver, M.D., member of Congress from Pennsylvania, who will speak on "A Doctor Congressman Looks At Politics and Issues For 1964."

Connecticut's U. S. Senator Thomas J. Dodd will speak on the role of professional men in politics. John Lupton, executive director, Connecticut Republican Citizens Committee, and Edwin H. May, Jr., former Connecticut GOP chairman, will talk about grass roots political and candidate support activities. State Representative J. McCullough Turner, of Bethany, who sponsored the animal research legislation adopted at the last session of the General Assembly, will also be among the speakers.

Activities of women in politics will be discussed by two members of the General Assembly, Senator Gloria Schaffer, and Representative Ina R. Vestal, both from Woodbridge.

The program will also feature workshops to study practical political problems and a question and answer session.

At 5:30 P.M. the program will conclude with a reception for physicians and their wives.

Doctor's Office

Anthony L. Dudzic, M.D., announces the opening of an office for the practice of psychiatry at 109 Broad Street, Middletown.

William H. Fisher, Jr., M.D., announces the opening of an office in association with Peter V. C. Dingman, M.D., and James M. Cary, M.D., for the practice of orthopedic surgery at 1211 West Main Street, Waterbury.

Jerome M. Hopper, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 50 Farmington Avenue, Hartford.

Luis M. Ramirez, M.D., announces the opening of an office for the practice of internal medicine and endocrinology at 635 Stratfield Road, Fairfield.

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BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Normal Psychology Of The Aging Process by Norman E Zinberg, M.D., and Irving Kaufman, M.D., International Universities Press, New York,. New York, 1963, 182 pp. $4.50.

Chemistry Of Thrombolysis: Human Fibrinolytic Enzymes by Kurt N. von Kaulla, M.D., Charles C. Thomas Publisher, Springfield, Illinois, 1963, 333 pp. $12.75.

The Thyroid And Its Diseases, 3rd Edition by James H. Means, M.D., Leslie J. DeGroot, M.D., and John B. Stanbury, M.D., with a chapter on Surgery of the Thyroid by Oliver Cope, M.D., McGraw-Hill Book Co., Inc., New York, 1963, 618 pp. $15.95.

Children Tell Stories, An Analysis Of Fantasy by Evelyn Goodenough Pitcher, Ph.D., and Ernest Prelinger, Ph.D., International Universities Press, Inc., New York, New York, 256 pp. $4.00.

Hospitals And Children Edited by James Robertson, International Universities Press, Inc., New York, New York, 1963, 159 pp. $4.00.

Your Child Step By Step Toward Maturity by Dorothy Noyes Sproul, Doubleday & Co., Inc., Garden City, New York, 1963, 274 pp. $4.50.

The Care Of The Geriatric Patient by E. V. Cowdry, Ph.D., The C. V. Mosby Co., St. Louis, Missouri, 1963, 566 pp. $11.85.

Mental Mechanisms by Henry P. Laughlin, M.D., Butterworth, Inc., Washington, D.C., 1963, 262 pp. $7.50.

Clinical Disorders Of The Heart Beat by Samuel Bellet, M.D., Lea & Febiger, Philadelphia, Pennsylvania, 1963, 1105 pp. $28.00

Atherosclerosis Mechanisms As A Guide To Prevention by Campbell Moses, M.D., Lea & Febiger Co., Philadelphia, Pennsylvania, 1963, 239 pp. $8.00.

An Atlas Of Congenital Heart Disease by Frank E. Sherman, M.D., Lea & Febiger Co., Philadelphia, Pannsylvania, 1963, 303 pp. $15.00.

The Electrocardiogram And Chest X-ray In Diseases Of The Heart by Arthur M. Master, M.D., Richard P. Lasser, M.D., Isadore Rosenfeld, M.D., and Ephraim Donoso, M.D., Lea & Febiger, Philadelphia, Pennsylvania, 1963, 565 pp. $21.00.

Special Notices

HARTFORD HOSPITAL
SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS

January 4 to February 29, 1963

January 4—Herbert Berman, Ph.D., Assoc. Research Prof., Boston, Massachusetts
Subject: "Anticoagulants and Thrombosis"

January 11—Ralph Alley, M.D., Dept. of Thoracic Surgery, Albany Med. Center, Albany, N. Y.
Subject: "Ventricular Aneurisms" (Dx and Rx)

January 18—Alan F. Guttmacher, M.D., Clinical Prof. of Ob-Gyn, Columbia P & S
Subjects: 10:00 a.m. "Methods of Contraception"
11:00 a.m. "Population Control"

January 25—Ben Spector, M.D., Coordinator of Anatomical Material, Harvard
Subject: "The History of Medicine Lives Again"

February 1—Harold M. Marvin, M.D., Assoc. Clinical Prof. of Medicine, Yale
Subject: "Heart Disease: A 40 Year Perspective"

February 8—Harry B. Harding, M.D., Assoc. Prof. of Microbiology, Northwestern
Subject: "Advances in Respiratory and Viral Infection"

February 15—Paul Calabresi, M.D., Ass't Prof. of Medicine and Pharmacology, Yale
Subject: "Antineoplastic Agents Useful in Non-neoplastic Disease"

February 22—Robert B. Greenblatt, M.D., Prof. of Endocrinology, Med. College of Georgia
Subjects: 10:00 a.m . "Recent Advances in Endocrinology"
11:00 a.m. "Dysfunctional Uterine Bleeding"

February 29—Stevenson Flanigan, M.D., Ass't Prof. of Neurosurgery, Yale
Subject: "Acute Management of Head Trauma"

Letter To The Editor

To the Editor:

Your editorial in the November issue of Connecticut Medicine titled, "Tale Of The Hippocratic Timber" should be made compulsory reading for every senior medical student and intern in our nation so that they become familiar, even if only in symbolism, with the great heritage of American medicine. I say this in spite of the fact that I am ordinarily not in favor of compulsion of any kind.

Maybe just "oldsters" like you and I appreciate these things. However, if we do not pass on our heritage to those who will follow us, I am fearful that the most honored profession will be the loser.

Sincerely yours,
Ellwood C. Weise, Sr., m.d.

Bridgeport, Conn.

NEW BOOKS IN REVIEW

SYNOPSIS OF ROENTGEN SIGNS by Isadore Meschan, M.A., M.D., W. B. Saunders Co., West Washington Square, Philadelphia 5, Pa., October 1962, 436 pp. $11.00.

Reviewed by: SIDNEY L. CRAMER

In the preface to this synopsis, the author stated that it was written primarily as an answer to the students who found the original "difficult to absorb in the limited time afforded." He had reference to a textbook of some fourteen hundred pages written by himself entitled, "ROENTGEN SIGNS IN CLINICAL DIAGNOSIS" published several years ago. In the latter, the author had used his own particular format for the presentation of the field of radiology, a form which will not be discussed in full within this report. Suffice it to say, outstanding within the book were the paragraphs of descriptive material which were concise, story-like and interesting to read. In this synopsis of four hundred and thirty-six pages, these descriptive paragraphs had been replaced by a format in which the primary and frequent roentgen signs of a particular disease appeared as lists of isolated sentences. In the oriignal text, the paragraphs mentioned above had provided "think time" between sentences so that the word picture unfolded itself gradually and made a more lasting impression. The lists of unrelated sentences seemed to the reviewer to be a mechanism for facilitating the memorizing of a large number of facts, but which held little promise for forming a solid foundation for the understanding of radiology. One imagined the superficial retention of such material until exam time and quickly forgotten thereafter. If this synopsis were the only text in radiology to which the student were exposed, and well it might be, it would not provide an adequate foundation in the fundamentals for future years.

Though too concise for the student, this feature made it valuable as an aid to the practicing radiologist. There was little question that the author was a busy radiologist in daily contact with physicians of all interests and exposed to the problems and queries of the various disciplines. In a few pages, he condensed related information which was frequently distributed in several textbooks. These included in addition to the roentgen characteristics, chief clinical findings, sites, pathology, skeletal manifestations, surgical techniques and clinical course. For instance, in discussing the subject of the healing of fractures, he made excellent use of the so-called "midget exhibit" which was a form of presentation unique to this author. This exhibit consisted of small line drawings thoroughly labeled and placed side by side to make comparisons and sequences easy to recognize at a glance. On a single page were shown stages of fracture healing including hematoma formation, periosteal reaction, callus formation, and bone resorption. In juxtaposition, on a facing page, a similar exhibit depicted the complications of fracture healing, including atrophy, non-union, etc., and even a cross-section of an extremity showing the relationship of the fractured bone to nearby muscles, tendons and nerves. These line drawings could then be compared with excellent reproductions of radiographs showing the described pathology. At the same time, to assist in answering the orthopedist's questions, was a description of the optimum angles of fixation at the various sites, the prostheses used, and drawings of their surgical application.

Because it would serve as a quick effective reference, this volume would be a valuable addition to the library of the practicing roentgenologist.

PRINCIPLES OF NEUROLOGICAL SURGERY by Loyal Davis, M.D., and Richard A. Davis, M.D., W. B. Saunders Co., Philadelphia, Pennsylvania and London, 1963 608 pp. $15.00.

Reviewed by: YALE D. KOSKOFF

This handbook is a concise nicely written well documented description of the specialty of neurosurgery. The emphasis is not on technique which can be found in such a book as Pappen's Atlas. It provides laboratory and clinical investigations in biochemistry, anatomy and physiological pathology as well as the various phases of electronics and instrumentation which are useful in neurosurgical diagnosis. It provides a good synthesis of neurology and neurosurgery.

The book is intended to familiarize the student and physicians with the facts of neurology both medical and surgical which would contribute to the best possible care of the neurosurgical patient. In its twenty chapters the authors have succeeded well in their purpose. They have brought forward with great clarity the newer contributions relating to such matters as vascular surgery of the brain and control of involuntary movements arising from disturbances of the extrapyramidal tract. They have not neglected the solid contributions of the past and have in a rather charming and original way introduced each chapter with a picture of the individual who may well be said to have made the most significant contribution in this field and whose name is associated with the subject under consideration.

After each chapter there is a short but pertinent bibliography which identifies the important contributions in the area under discussion. For this the authors are to be commended since they lay no claim to exhaustive study. While they modestly state that the book is intended for physicians and surgeons who wish to become acquainted with the principles of neurosurgery, the reviewer believes that the neurosurgical specialist will also find information and gain pleasure from reading it. There is a kind of charm in collaboration of a father and son in such a worthy enterprise. The senior author is a nationally famous teacher of neurosurgery and has done outstanding editorial work.

The publishers of this book deserve favorable comment because of liberal use of excellently presented illustrative material in such a compact form.

CHEMISTRY OF THROMBOLYSIS: HUMAN FIBRINOLYTIC ENZYMES by Kurt N. von Kaulla, M.D., Charles C. Thomas Publisher, Springfield, Illinois, 1963. 333 pp. $12.75.

Reviewed by: LOUIS H. NAHUM

This is the first comprehensive monograph on the mechanism of fibroinolysis in health and disease. This subject is important because of the mounting morbidity and mortality due to intravascular clotting. Apparently, more people in the U.S.A. are killed by intravascular clots than by malignant neoplasms, 343,926 against 260,047 in 1959. If we understood the mechanism of fibrinolysis in the human so that we could cause dissolution of intravascular clots, many patients who now die of this disorder might be saved by an appropriate preventive or therapeutic clot dissolving treatment.

The amount spent by government and voluntary agencies for research along these lines is pitifully small as compared to $113,514,528 for cancer research alone. A development and therapy testing program for clot dissolving agents is practically nonexistent. We need studies of all the factors concerned with deposition and dissolution of fibrin pathology within the body. The magnitude of this problem can be seen when we reflect that about two million in the U.S.A. are victims of cerebrovascular diseases due to thrombosis of blood vessels supplying the brain. And what about coronary thrombosis, thrombo-embolic disease, leg ulcers due to venous thrombosis?

There is much evidence that fibrin formation, and man removal of this formed fibrin, plays a very prominent part in human pathology and this extends into all branches of medicine. Atherosclerosis is thought by some to occur when fibrinolysis does not eliminate the small fibrin deposits in the artery wall. Fibrinolytic removal of fibrin in small vessels is important in the outcome of every inflammatory reaction.

This monograph then presents a discussion of actual problems related to the functioning and significance of the human fibrinolytic enzyme system with particular emphasis on the approaches towards thrombolysis and the presentation of the extensive results of the authors own researches. There is an excellent discussion of the history of the discoveries relating to the fibrinolytic enzyme system, changes in the trend of thinking in evaluating the significance of the various components of the system and prevailing thoughts up to the present.

The author rightly points to 1953 as a turning point in the study of fibrinolysis when Professor Daniel Kline of Yale purified plasminogen from human plasma. He details methods of measuring activity of the fibrinolytic system and its components. He evaluates every aspect both from the practical clinical point of view as well as these research elements. At the end he lists a host of unsolved problems remaining. The monograph is filled with ideas which when worked out will reveal the decisive role of the fibrinolytic enzyme system in the health of man, and thereby give the clinician mastery of a technique to dissolve clots by simple means. For this reason the design of the book is calculated to bring light to clinicians, researchers, biochemists and anyone concerned with the many aspects of the intact human fibrinolytic system. In this respect it is a very laudable and valuable effort.

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HANDBOOK OF PEDIATRIC MEDICAL EMERGENCIES by Adolf G. DeSanctis, M.D., and Charles Varga, M.D., The C. V. Mosby Co., St. Louis, Missouri, 1963 457 pp. $12.75.

Reviewed by: VICTOR L. SZANTON

The third edition of this useful book is well received. It has been thoughtfully improved: an enlarged volume with a handsome format of larger pages, new type without any sacrifice to legibility essential to the quick accommodation that its title suggests.

This edition brings up to date all of the information needed for emergency therapy. It is organized in a sound fashion, enabling one to find pertinent information promptly. Each of the fifteen chapters has a list of useful sub-headings. The largest of the sections is concerned with poisoning, a common problem.

The next largest one is excellent and is devoted to pediatric procedures. The photographs and directions are lucid and easy to follow. Those demonstrating internal jugular puncture for instance, together with the others, are probably in themselves worth the cost of the volume.

When the authors launch upon a fourth edition it is hoped they will also include cysternal puncture. Though little used, this procedure could be included with the other needle work delineated. A listing of poison centers, locations and telephone numbers would be helpful. It would be comforting to know, of the contributors, who wrote what. These suggestions are minor ones and are not meant to overshadow the enthusiasm that this volume engenders.

The seasoned pediat as well as the young physician can use this book. It achieves in exemplary fashion the purpose for which it was designed and is worthy of a place on the bookshelf of any physician who takes care of children.

REVIEW OF MEDICAL PHYSIOLOGY by William F. Ganong, M.D., Lange Publications Los Altos, California 1963., 577 pp. $6.50.

Reviewed by: LOUIS H. NAHUM

The author of this review is Associate Professor of Physiology at the University of California School of Medicine, San Francisco. He has provided a concise summary of mammalian and particularly human physiology which medical students can use with great profit. Physicians can use it also as a review in which are discussed important symptoms produced by disorders of function. If one reads it as a review one realizes that it cannot be complete and concise in every detail and because it is a summary one should not label it as dogmatic. In fact, the conclusions presented by and large are supported by the bulk of currently available experimental evidence.

There are forty chapters, an appendix and an index covering every aspect of physiology, beginning with an overabbreviated chapter on physiologic principles which cover body composition, the capillary wall, cell membranes, pH buffers and homeostasis. Each chapter is followed by basic references. The book is an excellent review and fully meets the purposes for which it was intended. It will be of great help to students, house officers and physicians generally.

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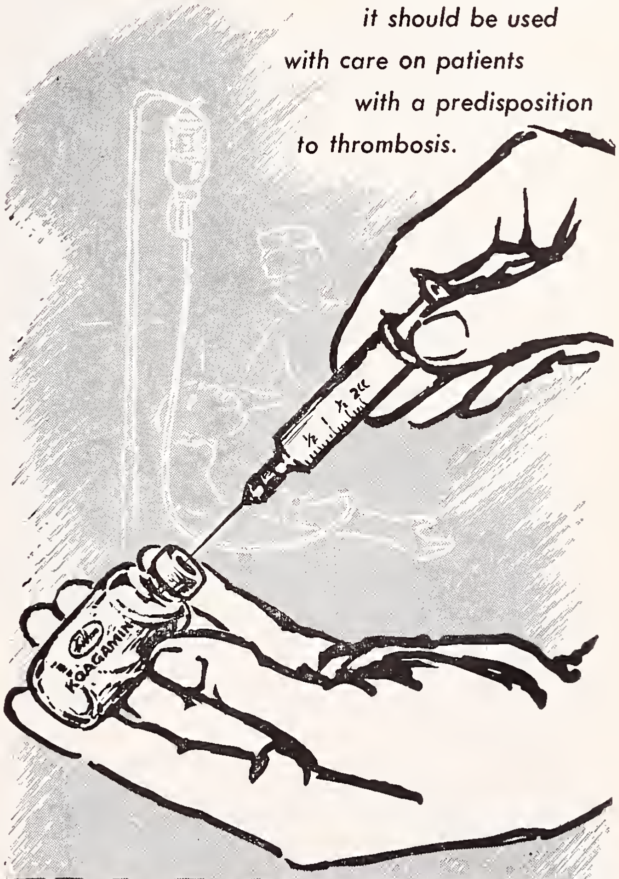

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Warning: May be habit forming.

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SPECIFIC AND NON SPECIFIC FACTORS IN PSYCHOPHARMACOLOGY by Max Renkel, Editor, Philosophical Library, Inc., New York 1963 174 pp. $3.75.

Reviewed by: LOUIS H. NAHUM

The title of this book is very expressive of its contents. For in an extended first paper by Himwich one of the pioneers in psychopharmacology, we are given a review of the brain amines serotonin and nor-epinephrine. How they may be made to accumulate by monoamine oxidase inhibitors and how they may be depleted by reserpine. Their accumulation leads to psychotic states, their depletion to depressive ones.

The remaining portion of the book is devoted to the nonspecific factors. The recognition of these factors was forced upon those concerned with the future of psychopharmacology because powerful drugs have been produced in profusion and their use has led to widespread disagreement as to their true value. Some excellent observers report excellent results and other equally reliable scientists report disappointing results. It soon became apparent that there was no quantitation in this field and without it one could not expect uniformity in results. Beecher presents a scholarly plea for methods to obtain measurements of the dosage and effects of drugs and there follow studies by Knight on sources of error in assessing drug response by Lasagna on the relation of drug induced changes to personality. There follows another paper by DiMascio and Renkel on personality and drugs; one by Malitz on variables and drug effectiveness.

The one by Feldman on the role of the physician and his attitudes is an especially revealing study, because it emphasizes that investigations show great variability. One type will report significant improvement in drug trials in 93 per cent; one type in 44 per cent and a third type in 4 per cent. Most of those whose results were unimpressive regarded resorting to chemotherapy as an admission of incompetence or lack of faith in psychotherapy. These were most ardently identified with psychoanalytic principles and felt they were losing face or being unfaithful to the principles of dynamic psychiatry by indulging in pharmacotherapy! It is clear we need someone to appraise the appraisers.

This book clearly reveals psychopharmacology is here to stay but much more work is needed to quantify the results, to eliminate bias in "objective" estimation of the host of drugs which are descending upon the profession like a deluge and to recognize the non specific factors in their measurements.

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PHARMACOLOGY REVIEW: 1200 Multiple Choice Questions and Answers by Maurice B. Feinstein, Ph.D., Medical Examination Publishing Co., Inc., New York. 1962 173 pp. $4.00.

MICROBIOLOGY REVIEW 1500 Multiple Choice Questions and Answers by Charles W. Kim, Ph.D., Medical Examination Publishing Co., Inc., New York, 1962 206 pp. $4.00.

Reviewed by: LOUIS H. NAHUM

Both of these books are completely referenced and the answers can be found at the end of each one. Each gives references to textbooks where complete answers can be found. It is clear that the Editors have taken great pains to thoroughly check the questions and answers but if at all in doubt, the reader is urged to consult the references.

This basic science series is of inestimable value to the student who is preparing for the National Boards. But it will be a source of great satisfaction as an intellectual exercise for all physicians who wish to know how up-to-date this knowledge is and where they must do some reading urgently. It will surely reveal many weaknesses in some of the areas of knowledge and clearly indicate those fields where further study is needed. It is certainly better to expose your weaknesses to yourself in order the better to reveal knowledge to others. This whole series is heartily recommended to all medical students and practitioners who aspire to remain students in medicine.

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Connecticut Medicine

Connecticut State Medical Journal

Volume 28 / February 1964 / Number 2

LABORATORY MEDICINE ISSUE: ROY N. BARNETT, M.D., GUEST EDITOR

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SEMMELWEIS: DEFENDER OF MOTHERS (see page 81)

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editorials

The Smoking Report

> *Mortals blame all their ills on us, says Zeus, but they suffer beyond necessity through their own foolishness.*
>
> —Odyssey

It is now official. What this department described under the title "Smoking And Physiological Age" in 1962 is recognized as true. The Surgeon General's Advisory Committee on Smoking and Health has declared that there is a definite causative link between lung cancer and other major diseases and the continued use of tobacco. Bluntly stated smoking is harmful to health and remedial action must be taken.

The Federal Government's ten-man panel has come to this conclusion after an objective and careful study of many thousands of scientific reports. The overwhelming evidence is that smoking especially of cigarettes is the main factor in the increase in lung cancer;[3] that heavy smoking is a cause of other pulmonary ailments; that there is further evidence connecting smoking with heart, circulatory and other diseases, a fact also published in these pages[1] and that smoking by pregnant women affects the weight of their babies. The American Cancer Society has long ago concluded that the risk of developing lung cancer is directly related to the number of cigarettes smoked; the American Heart Association long ago concluded that coronary heart disease or its complications are higher among heavy cigarette smokers. The conclusions of the United States Public Health Service are confirmed. So also are those of the Medical Research Council of Great Britain, the Royal College of physicians of London, the Public Health studies of other European Nations and of Canada, that excessive smoking not only can, but actually, does lead to an earlier death, estimated as eight years sooner in one who smokes twenty cigarettes a day and sixteen years sooner in the one who smokes forty cigarettes a day. Calculated in a more specific way, every cigarette smoked, destroys fourteen and one-half minutes of the smoker's life.[2]

The bold and devastating report of the Surgeon General cannot be ignored by cigarette, pipe and cigar smokers, young or old, nor can the smoke be "blown away by the tobacco industries spokesman" or the wishful thinking of even some pathologists. The objectivity of the panel, is eloquently attested when one reflects that several were seen to smoke cigarettes during their appearance on television. Now it cannot any longer be maintained that only non-smokers accept the validity of the harmful consequences of smoking. There is no doubt that as the Surgeon General promises, the Public Health Service will recommend appropriate further action. The inevitable pressures upon Congress and other concerned Fereral agencies will make it too difficult for them further to evade their own responsibilities in this field. There will be expected to develop anti-smoking campaigns. Doubtless these should be directed first and foremost to the nation's youth where the habit first breeds.

THE COVER

SEMMELWEIS: DEFENDER OF MOTHERS

HUNGARIAN PHYSICIAN Ignaz Philipp Semmelweis (1818-1865), while Assistant at the First Obstetric Clinic of Vienna's great Allgemeine Krankenhaus in 1847, discovered means of preventing puerperal fever: he insisted that physicians and medical students wash their hands in chlorinated solution before entering obstetric wards and again before examining each patient. His rule was much resented and opposed—but hundreds of mothers' lives were saved. Though his doctrine was proved repeatedly, both in Vienna and in Budapest, most of his contemporaries opposed it; and, both depressed from worry and brokenhearted from disappointment, Semmelweis died at age 47, of blood poisoning, the infection he had fought so valiantly to prevent in his patients.

Downright prohibition is unthinkable and probably wrong. But is there not some way of regulation by proper government agencies as they regulate other industries with health hazards? Is it not time that this country should take its place with Great Britain, the Soviet Union and Denmark whose public health ministries already use posters and other means to warn against smoking? Should we not enforce laws on the state and municipal level against sale of cigarettes to minors? Is it right for hospitals which exist for the defense and restoration of health to participate in the sale and distribution of cigarettes?

However, public education and appropriate legislation will be ineffective unless physicians and parents play a major role in helping to safeguard the health of children and of patients who have already fallen victim to this most pervasive and potent form of poisoning. This is one way to safeguard the nation's health. Is this not what the smoking report is really all about? As the *New York Times* has so aptly put it "Public health is a public —and a private responsibility." In this area the health professions should accept leadership.

L.H.N.

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Interferon

Most patients eventually recover from virus infections. Since we have as yet no antibiotic against them, perhaps, if we knew the factors that are responsible for the recovery, we might be enabled to gain mastery over them by rational rather than by biochemical means. We know that during the course of a virus infection antibody develops in the blood and may remain for variable periods of time sometimes for life, as in the case of measles. This antibody is able to combine with any measles particle that infects the patient at a later date and thereby prevent a second infection. The success of virus vaccines in protecting against smallpox, yellow fever, and poliomyelitis is compelling evidence of the ability of antibody to protect against virus infections.

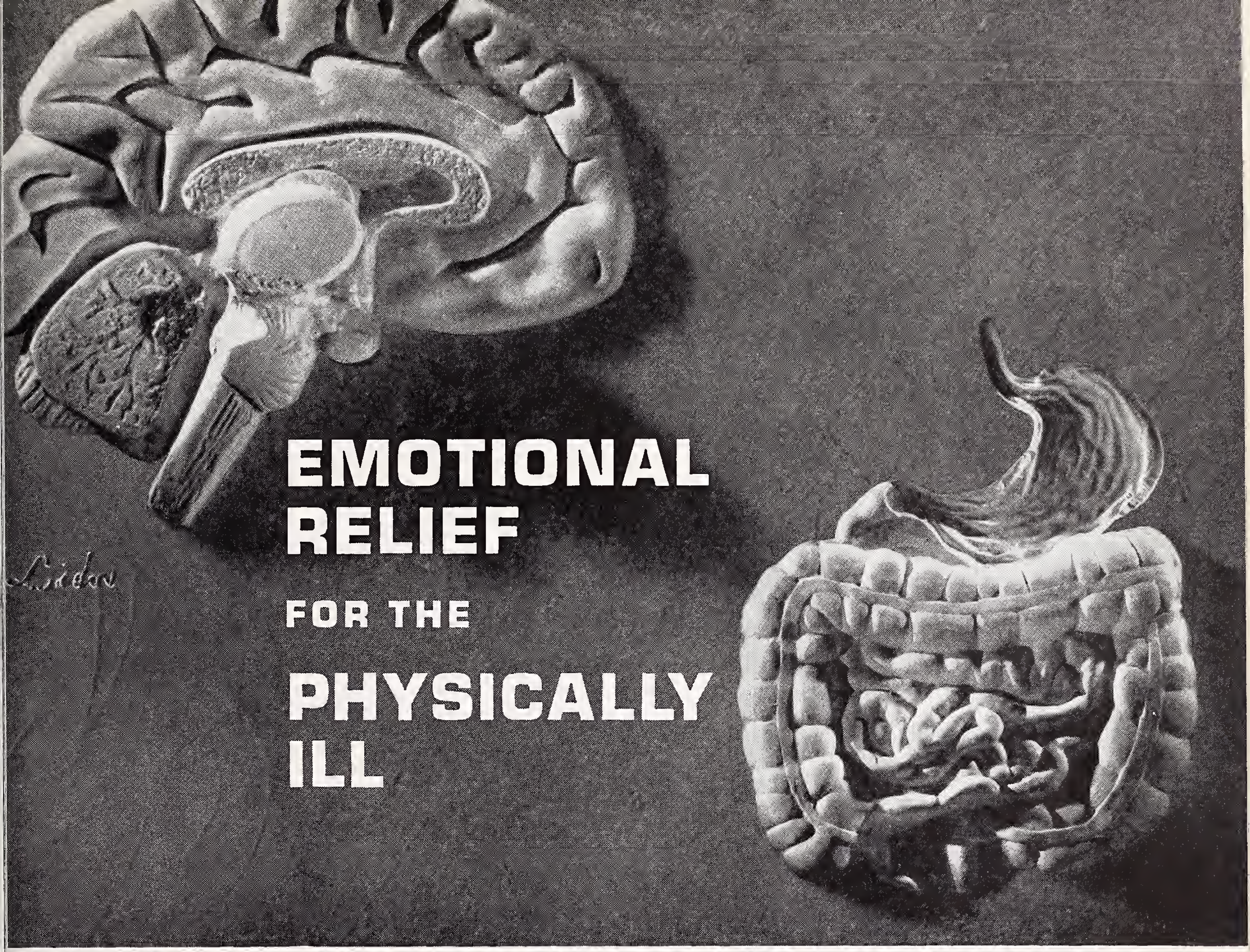
Antibody however, combines with viruses outside cells, normally does not enter cells, and only appears usually quite late in an infection when the recovery process is already well underway. It is therefore not expected to halt an infection by a virus like vaccinia that first enters a cell and then spreads from one cell to another. Furthermore, recovery from virus infections occurs in such conditions as hypogammaglobulinemia and animals treated with x-irradiation in which the patient or animal is incapable of making any significant amount of antibody. It would seem as if antibody is a by-product of a virus infection but does not play a dominant role in recovery from a virus infection.

This fact is well known to virus workers in the laboratory who study individual cells infected with certain viruses in the test tube. In such a model system, after a period of virus multiplication during which some cells may be destroyed, the majority of cells recover. Since no antibody is present in these experiments, this focuses attention on cellular factors in the recovery process. Isaacs[1] has shown that under the stimulus of virus infection, cells respond by producing an antiviral substance which he has called Interferon.

Interferon production seems to be a very general response of cells of many different vertebrate animals from birds, rodents, carnivorous up to man, and it occurs with cells from many different organs of the body. It is also a response to infection with large numbers of different viruses, although some strains of virus are more effective than others at stimulating cells to make interferon. In short, interferon production is a cellular immune response to virus infection in contrast with antibody production which is a feature of thymo-lymphatic cells which respond to the entry into the body of foreign antigen, particularly protein.

The effect of interferon is to induce a temporary resistance to virus infection in the cells surrounding those first infected. In this way interferon limits the spread of a virus infection and could play a role in the process of recovery from virus infection. Isaacs points out that interferon seems to act by inhibiting an oxidative process that supplies the energy for viral synthesis. If this were true then its antiviral action is not specifically directed towards the virus that induced its production but rather towards its viability and multiplication.

It appears that the interferon mechanism only begins to function normally after the first third of embryonic life. The cells of very young chick embryos produce little interferon and are also insensitive to the antiviral action of added interferon. This seems also to be true of mouse embryos. It is not known whether this is true of human embryos, but if it were, it might partially explain why mothers infected with Rubella virus during the first trimester of pregnancy sometimes give birth to



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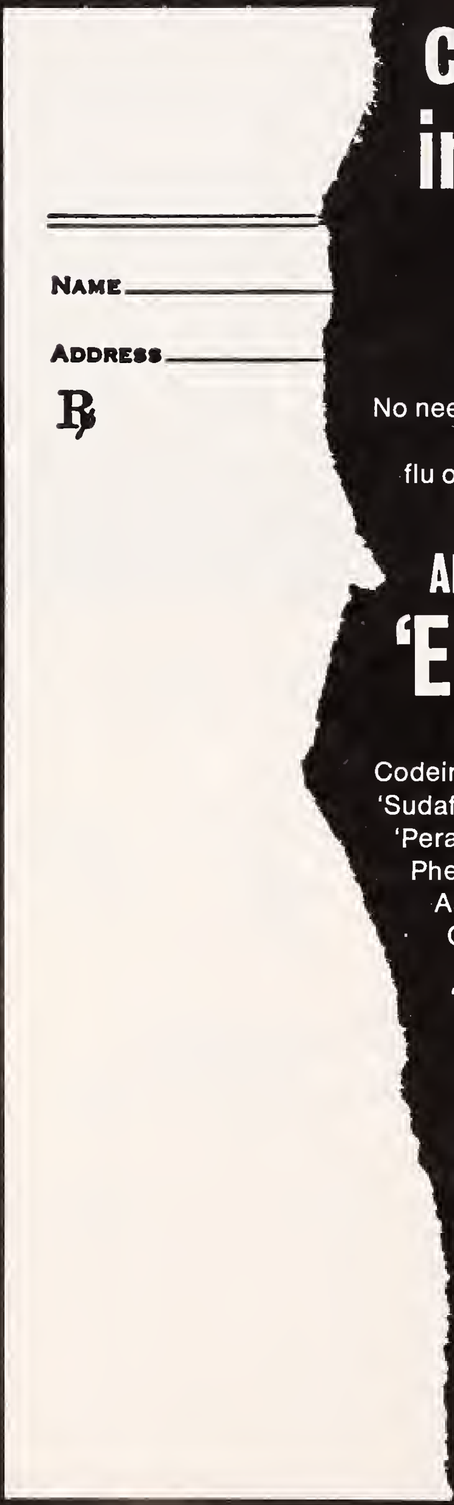

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babies with congenital abnormalities. This phenomenon is extremely rare when the infection occurs after the third month of pregnancy. However, once there has developed an actively functioning interferon mechanism, animals also develop ability to recover from virus infection.

Two ways of blocking the interferon mechanism have come from test tube experiments. One was by raising the oxygen level in the atmosphere of the cell cultures. If interferon blocks oxidative metabolism of the intracellular virus, then one might expect a higher oxygen supply to interfere with the interferon actions and this was in fact demonstrated by Isaacs. We might expect a similar result in an animal infected with influenze virus if they are kept in an atmosphere of 50 per cent of O_2 concentration which in itself is not harmful. This in fact was also found to be true in mice which under the above experimental conditions showed an increased mortality and earlier deaths than in the control animals. The opposite should also be true namely mice similarly infected and kept in a lowered oxygen atmosphere should survive longer than control animals and they do. Such findings of course, make us wonder about the routine treatment of viral infections of the respiratory tract especially in infants by placing them in an oxygen tent. This is an admittedly complicated subject, because there may be cases suffering from oxygen lack in which the supply of oxygen can save lives.

A second way of inhibiting the interferon mechanism in the test tube experiment is by the use of cortisone. This is a relatively recent finding but it fits well with clinical and laboratory evidence that cortisone can have a harmful effect on the course of a number of viral infections. All in all the evidence seems to point to the interferon mechanism as probably playing an important role in our ability to recover from virus infections. When in our clinical practice we do things that may overcome the interferon mechanism, such as high oxygen administration or cortisone therapy then we may be preventing recovery from virus infections.

These are surely the negative side of recovery from virus infections. There must be positive factors that assist the interferon mechanism. Here again we receive guidance from studying cell cultures. By raising the temperature of the cultures or the experimental animal, they can be cured of polio virus infection. The question of course, was whether the raised temperature operated by favoring the production of interferon or whether it acted by a totally different mechanism. This question has not been finally answered. Nevertheless, this observation has great clinical implications. It indicates clearly that we must be wary of treating our patients with fever caused by a virus infection by efforts to reduce the temperature such as the use of salicylates or sponge baths. The patients are probably better off with their fever.

The temperature may be an important factor in whether interferon production is accelerated or retarded or stated in another way, whether the virus will multiply or fail to do so. Many "cold" viruses grow well at 33° but not at 37° and are at the same time very sensitive to the antiviral action of interferon at body temperature. Perhaps this is why most of us recover quickly from virus colds, especially if a fever is developed at the same time.

It is natural to wonder whether we can make use of interferon in a more direct way as we use antibiotics in bacterial infections, that is by giving it to certain patients. The answer to this question is not yet at hand. For the present, an alternative and perhaps a more logical course is to try to find some method of stimulating people to increase their own production of interferon, or their sensitivity to its antiviral action. What is already clear is that the model system of studying virus infected cells in culture, promises to be an interesting and important field for research.

L.H.N.

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Hyperimmune Gamma Globulin: 1. A New Dimension In Immune Therapy

In any long range view on the elimination or prevention of various diseases we can no longer lose sight of the uses and value of hyperimmune human gamma globulin. We have known for a long time that gamma globulin provides prophylaxis of short duration or therapy but recent knowledge shows that there may be uses to assist in active immunization as well. The demonstration that passive protection against paralytic polio could be achieved with immune gamma globulin in both animals and man gave some assurance that active immunization would prove successful, for it signified that the infective agent stimulated the formation of hyperimmune gamma globulin. The antibodies present in human gamma globulins are all a result of accidental or deliberate contact with infective agents and other antigens.

In the past few years important data has been accumulated on the effect of hyperimmune gamma globulin in the therapy of malaria in children in the Gambia. The process of constant re-infection in endemic regions results in an impressive hypergammaglobulinemia as compared with persons not infected, or those who took antimalarial drugs. This hyperimmune gamma globulin produces a sharp reduction in trophozoite counts[1] and after elimination of the parasite, the children are protected for a period of three months and then become susceptible to reinfection. This is a clear demonstration that humoral antibodies play a role in immunity to malaria, and should stimulate a search for a vaccine for active immunization as it has in polio and measles. But before this can be accomplished we need to learn the stage in the life cycle of the parasite against which the gamma globulin is effective, so that cultivation and active immunization can be achieved. Without doubt these results with malaria will stimulate parallel studies to evaluate the effects of gamma globulin on other diseases in which gamma globulin is high in persons living in areas infected with kala-azar, trypanosomiasis and toxoplasmosis. At any rate the discouragement as regards active immunization against parasitic diseases may give rise to optimism as these studies on hyperimmune gamma globulin continues.

A most important way in which hyperimmune gamma globulin can be of value is in the prophylaxis and treatment of tetanus. The hazards of horse-serum are now well established and should make this product completely unnecessary with so many persons actively immunized by toxoid.[2] All that is needed is an effort to increase the production of human antitoxin.[3] Perhaps the Red Cross and other blood collecting agencies could give an injection of toxoid at the time of blood donation as a way of augmenting the supply of hyperimmune gamma globulin.

A considerable body of evidence suggests that hyperimmune gamma globulin from subjects four to eight weeks after vaccination or from convalescent cases of smallpox is of great value in the prophylaxis and treatment of smallpox, generalized vaccinia, vaccinia gangrenosa, eczema vaccination and especially in the treatment of postvaccinial encephalitis. The antibody levels in serum of persons convalescing from smallpox was 20 to 100 times higher than even in those recently vaccinated subjects. But since smallpox vaccination is generally required in the United States and this source of hyperimmune gamma globulin is non-existant, antivaccinia gamma globulin should be important in therapy of severe complications of vaccination.

There is now a possibility of assaying the potency of ordinary and convalescent phase gamma globulin against rubella. Phophylaxis against this infection is of primary importance because of the known high incidence of congenital malformation in babies born to women contracting rubella during the first trimester of pregnancy. However, the virus is now available and the possibility of preparing a vaccine, creating a hyperimmune gamma globulin or deliberately inducing rubella prophylactically should help avoid the dangers associated with contracting the disease during pregnancy.

Through the use of hyperimmune gamma globulin it is possible to reduce the incidence of orchitis in mumps[4] by three fold. Gamma globulin is now being prepared from serum of artificially immunized donors and assayed by the potency of the anti-serum in inhibiting hemagglutinins of red cells by the mumps virus. We need to learn the potential needs of this preparation in relation to its supply.

As regards bacterial infections particularly those responding poorly to antibiotics alone, such as the staphylococcus and proteus, the combination of hyperimmune gamma globulin plus antibiotics may be beneficial. Especially in burned patients there has been reported a reduced incidence of septicemia and of late death as compared to antibiotic therapy alone, but very large doses of the gamma globulin were required. Much more studies are needed for each organism and by the double-blind method, especially for organisms such as the staphylococcus, Escherichia coli and proteus. There is also a need for adequate methods of evaluating the protective antibody content of different batches of gamma globulin by tests that measure protective antibody. Perhaps when we learn which antigen of the staphylococcus it is that is associated with protection, such a development might lead to the production of hyperimmune gamma globulin and to active immunization.

This development of the uses of hyperimmune gamma globulin both in passive and active immunization has added a new dimension in our conquest of infectious disease.

L.H.N.

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Salt, Genetics And Hypertension

Sodium became an important subject in the treatment of hypertension after it was recognized in 1957, that natriuretic compounds are quite efficient in reducing blood pressure in at least one-third of all patients treated. It must be admitted however, that long before this period, Ambard and Beaujard (1904) speculated on the possible role of salt in hypertension, just as Allen in 1922 hazarded a guess that general abstaining from salt would probably be associated with a reduction in the morbidity and mortality from renal and vascular disease. However, he was reluctant to suggest such a treatment in general because of the possibility that salt ingestion was based on a deep instinct and that to tamper with it might lead to unfortunate results.

We have known since ancient times that salt has been added to food by man. It is now so widely used, and with such little restraint, that it is easy to assume that large amounts are clearly necessary. But is this assumption dogma or truth. A glance over other parts of the world show that there exist numerous people which for untold generations never added salt to food and ate only that which was contained in natural food stuffs. The Eskimos, the northwest American Indians and the Masai of Africa, living in markedly different climatic geographic and cultural environments, ate less than five grams of salt per day and some were eating less than one gram per day. By contrast most of us consume two to five times the maximal intake of these primitive peoples. How much then do we really need under ordinary circumstances?

There can be no question that the body needs some salt, since sodium is the major cation of our blood and extracellular fluids. In the past, estimates as high as fifteen grams per day have been made, although this is now known to be excessive. Can it be that the real optimum dose of salt eaten by primitive peoples is closer to the maximum than what is ingested by "so-called" civilized people. Only careful, controlled metabolic studies, on ambulatory healthy patients can separate dogma from fact. Dahl[1] found that the minimal daily requirements for sodium are actually less than one gram per day. Indeed it might even be less, since he cites evidence which has just come to light that some of the natives of Dutch New Guinea appear to have had life-long intakes of only thirty to seventy milligrams of salt per day. These observations of course, do not necessarily imply that such low salt intakes are either necessary or advisable for our general population, but they serve to illustrate the fact that the common practice of adding salt to our food, whether harmful or not, probably is generally unnecessary.

If daily sodium intakes of about one gram normally are adequate, why then do most adult members of western societies consume ten to twenty times this amount? The issue is not whether salt appetites exist (they do) but whether these appetites are innate or acquired. Dahl believes strongly that the appetite for salt normally is acquired rather than instinctual, much like the appetites for tobacco and alcohol. If the appetite for salt is acquired, then most of that consumed is unnecessary. If this is so, is it potentially harmful? Dahl comes to grips with this question having collected statistical data and performed careful experiments on rats.

When one correlates data on salt intake among several groups throughout the world, with the prevalence of hypertension, a striking relationship was uncovered. The Alaskan Eskimos, whose salt intake is less than three grams per day, exhibit no hypertension; the American with a salt intake of ten grams per day show ten per cent hypertension; while some Japanese who consume twenty-six grams of salt per day show thirty-eight per cent of hypertension. When Dahl fed rats varying amounts of salt, he found that what was true of human feedings was also true for rats, since with increasing average salt consumption, there appeared to be a parallel rise in the frequency of hypertension. The experimental hypertension in rats bears a close resemblance to the human variety. For instance the onset may occur at varying ages, that is, at different intervals after the onset of salt feeding. Once present, the hypertension rarely if ever disappeared as long as the salt was continued. The elevation in pressure was slow to appear and progressed slowly. It might plateau at a modest level or advance explosively. The responses ranged from none to rapidly fulminating hypertension and death. Finally, once hypertension is established, it disappeared only in about one-quarter to one-third of the animals, just as the human variety does after salt is eliminated.

There is a recognized association between obesity and hypertension. Here the problem is more complicated than just the fact that people who ingest more calories also ingest a proportionately greater amount of salt. Lipid and carbohydrates metabolism must also be taken into account. Nevertheless, it is undeniable that obese people must ingest more salt than average people. Furthermore, drastic calorie reduction in such patients frequently result in a fall in the elevated pressure during the first few weeks on a low calorie diet before any significant weight loss has occurred. This precise pattern of response also occurs in some hypertensive subjects on low sodium diets. Stated another way, perhaps it is the curtailment of salt, rather than the weight loss, that was the effective means of lowering blood pressure. Dahl tested this hypothesis on obese hypertensive patients and uniformly observed that calorie restriction without salt restriction failed to lower blood pressure. Clearly it is the salt restriction which plays a major role in lowering blood pressure in obese individuals with hypertension.

If sodium is an etiologic factor in human essential hypertension, should it also be found in increased concentrations in the tissues of hypertensive animals and man. The answer to this question is not at present clear cut. The evidence is conflicting. However, studies with radioactive Na_{22} suggest that sodium is eliminated at a slower rate in hypertensive than normotensive individuals and this finding suggests a greater sodium pool in hypertensive patients. Of course, this still doesn't answer the basic question whether any excess tissue sodium was causal to or a result of the hypertension. Furthermore, if the chronic excess salt ingestion is a cause of hypertension, then why doesn't every person or rat eating large quantities become hypertensive, since we all know persons who are heavy salt eaters, yet remain normotensive. The same is true with the rat.

This suggests of course, that these marked differences in response to salt are controlled in some way by genetic factors. If this is true, one ought to be able by the technique of selective inbreeding in rats, to obtain some strains which will develop hypertension by excess salt consumption. Dahl achieved this objective and obtained a strain resistant to salt in successive generations and another strain that rapidly develops severe and fulminating hypertension on a high salt diet. It is of very great interest that the sensitive strain, if denied excess dietary salt also failed to develop hypertension. Thus a strain genetically predisposed to hypertension, appeared to need the additive environmental factor of dietary salt in order for the hypertension to develop.

It seems reasonable to expect that similar genetic factors operate in man. The usual genetically heterogenous population characteristics in man would make it illogical to expect that all individuals on similar salt intakes should have similar blood pressures. On the contrary, one would expect to find individuals in a high average salt intake who did not develop hypertension as well as individuals on lower average salt intakes who do develop hypertension. However, both human and experimental data suggest that individuals on a life long low salt diet rarely develop essential hypertension.

From the standpoint of the practicing physician, the data are pertinent, since they indicate that in families with a history of hypertension, it may be wise to limit salt intake from early childhood, before, rather than after hypertension develops.

L.H.N.

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Microbes And Man

With the introduction of antimicrobial agents during the third and fourth decades of this century it was generally supposed that the contributions of the field of microbiology to practical medicine had reached their height. Fortunately, this view has proved to be wrong and the study of germs has continued unabated, a circumstance vital for man's future. The immediate reason, of course, was the appearance of drug resistant bacteria, a circumstance that might have been inferred from an extension of Darwinism laws to bacteria. Another reason is the fact that one large group of microbes—the viruses—has remained almost entirely unaffected by the substances so far brewed or synthesized. Another reason is that after an infection has taken place, the successful use of chemotherapeutic agents to eradicate the culprit, unfortunately still gives it an opportunity to disseminate its kind. Thus there remains abundant tasks to challenge the talents of the microbe hunters in improving prophylactic procedures and discovering new ones. They have not been too slow in this task as witness the recent progress with attenuated vaccines for measles and poliomyelitis. They are searching for additional therapeutic agents. They are uncovering etiologic relationships for some of the commonest affections of mankind as exemplified by the current studies of the acute respiratory diseases.

A very important area of the studies of the microbiologist is in the field of heredity of single cell organisms. These are opening broad vistas of understanding in respect to the meaning of the "gene" in its chemical as well as its biologic sense. In at least one instance of a human disease of heredity—galactosemia, the metabolic error in affected infants —the absence of phosphogalactose—uridyl transferase has been claried by investigations of the same enzyme system in bacteria.[1]

From microbiology has come an acquaintance with several possible causes of alterations of genetic substance in bacteria, which may also turn out to occur in man. One of these is known as "transformation" which depends on the transfer of deoxyribose nucleic acid (DNA) of one cell to

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another. How this molecule penetrates the cell membrane is not known but there does result a persisting alteration in some characteristic of the recipient organism. Up to this point this transformation has generally been a laboratory induced process, but there is some evidence that it may occur spontaneously.

A second route of genetic transfer is termed transduction. In this case a latent virus infecting one bacterium may pass to another carrying with it—on its back so to speak—some of the gene substance of the first. Another process also depends on viral infection of a bacterial cell, but it causes a latent infection, one in which the viral neucleic acid may participate in the activities of the cell, causing it to do something new. An excellent example is the discovery that diphtheria toxin can only be produced by a diphtheria bacillus which is infected by a special virus. Without this infection the diphtheria bacillus will not produce the toxin.[2] Numerous other examples of new characteristics in animals and plants caused by viruses are now well documented.

The viral infection may not be latent, but overt. The nucleic acids of the parasite subvert the normal physiologic processes of the affected cell to the end of producing more of the parasite. This process gives us a clear model that we may apply to the understanding of viral infections of man.

We have been in the habit of thinking that when a modification occurs in a living organism that is reproducible from one generation to the next that it occurs randomly as a result of forces unknown. The revelations from microbial studies reveal that genetic modifications may occur in several already known ways, and this knowledge may prove in the long run to give us some insight into the incipience of neoplasma, as well as power ultimately to control hereditary characteristics at will.

Virus induced tumors of animals have been known for many years including such well documented examples of Rous sarcoma of chickens and myxoma and fibroma of rabbits. The recent discovery that a single such agent, the polyoma virus can cause any of a variety of tumors in several species of laboratory animals including the mouse, hamster and rat is even more suggestive of the human situation. This same virus it appears may provoke leukemia as well as a variety of solid tumors including those of skin, mammary tissue, lungs, gastrointestinal tract and salivary glands.[3]

In the light of the several known modes of genetic shuffling learned from microbes, we may envision the onset of neoplastic growth through the already familiar mechanism of latent or overt infection by viruses or by the more subtle related concept of transduction in which there occurs an invasion by a virus, which itself remains latent, but brings into the cell, genes which are out of place and provoke unnatural activities such as uncontrolled cell multiplication. Or we may envision it in terms of transformation—in which there is a direct transfer of inappropriate gene substance from cells of the subject itself.[4] The prospects opened up to us by these various possibilities are manifold. Pursuit of them is almost bound to clarify general problems in the genesis of growth, even though they turn out to be inapplicable to the etiology of cancer in man. There is, however, no reason to place man in a separate category from other creatures certainly as far as the operation of the genetic apparatus is concerned.

In one other area the body of knowledge of intermediary metabolism, we owe a great deal to the study of these processes in microbes. Microbes build and metabolize glucose, lipids, amino acids, vitamins, etc. . . .Accordingly, much has been learned from them about the channels of glucose oxidation, utilization of amino acids and synthesis of lipids. At least one well known vitamin paraminobenzoic acid was discovered in studies of bacteria and another of much importance to treatment of pernicious anemia, Vitamin B_{12} is produced for commercial purposes by a bacterium and is assayed by others which fail to synthesize it.[5] These are but a few instances of a wide variety of analogous revelations.

As the nature of biologic phenomena becomes clearer, we begin to recognize the unity that exists in nature. Microbe and man operate on the same fundamental biologic laws. It is possible to become excited about what happens in a bacterium or virus because such studies can make basic contributions to clinical medicine in the practical realm of therapy and help formulate an intellectual climate which will some day help solve the riddles of health, resistance to disease, inheritance, and cancer.

L.H.N.

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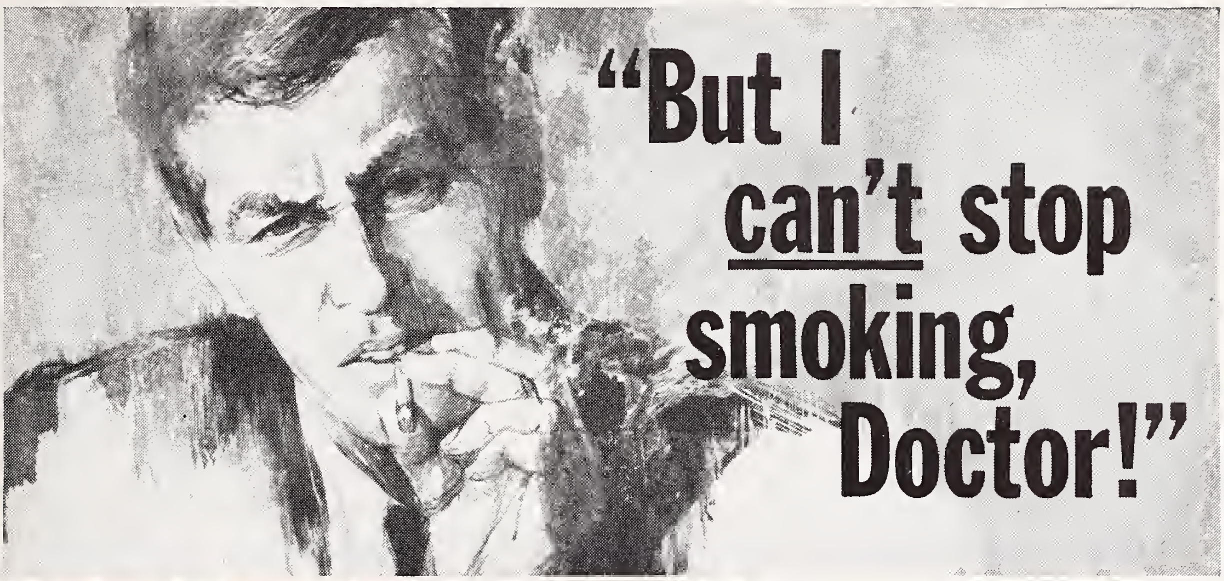

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Progress In Vascular Surgery

To discover the etiology of arterial disease is an extremely important endeavor because it might lead to its prevention in future generations, or its arrest in the present, thereby, eliminating the most common cause of death and disability and avoid much human misery and wastage. But the time is here and now, and the task is also to do what we can to eliminate whenever possible its crippling effects upon people. It is therefore, not surprising that the Lasker Award has recently been bestowed upon Dr. Michael E. DeBakey who has contributed so much towards the surgical correction of arterial obstructions.

Dr. DeBakey has been associated not merely with the development of relatively safe and readily applied methods of angiography, which has permitted roentgenographic visualization of the arterial tree, but also with the development of highly successful methods of vascular surgery, including the use of vascular replacements. These have resulted in a tremendous surge of interest and increasing intensity of research endeavor, both clinical and experimental. As a result, certain concepts have been developed concerning diseases of the aorta and major arteries that provide the basis for rational and effective therapy. It has become clear from studies along these lines, that regardless of etiology, the lesion in many forms of aortic and arterial disease may be well localized and segmental in nature with a relatively normal patent proximal and distal arterial bed. It is this fortunate aspect of the pathologic-anatomic nature of arterial disease which now enables the surgeon to "leap across" the obstruction and achieve the ultimate objective of effective therapy—the restoration of the circulation to a deprived area.

A deprived area in principle, must remain viable even though certain degrees of ischemia may inhibit normal function. Only if the tissue is viable, can a restoration of circulation lead to return of normal function. Viability therefore, is dependent upon the existence of collateral channels sufficient to keep the tissue alive but in which normal function is temporarily inhibited. With angiographic studies the collateral circulation can be visualized and one may reasonably expect a return to normal function after overcoming the major obstruction in the presence of sufficient collateral circulation.

The primary objective of therapy—the restoration of a normal circulation by removing a segmental obstruction therefore, consists essentially of thromboendoarterectomy, excision with graft replacement by bypass graft or patch graft angioplasty. A most important consideration in the development of a satisfactory and effective arterial substitute was first an arterial homograft, but the author encountered a number of disadvantages in procurement, preparation and inadequate availability. Furthermore, in some instances degenerative mural changes led to late complications. For this reason efforts were directed towards development of an arterial substitute which would be free of these disadvantages. Long trials and tribulations finally led to the development of a flexible, seamless, knitted Dacron tube, which was found to meet the essential requirements of strength, durability, and function.

DeBakey reports his experience with this graft replacement in over 5,000 cases and extended over a period of eight years. Long term studies have clearly demonstrated that the tube becomes readily incorporated in the body with the development of an intimal lining that simulates both histologically and functionally the normal arterial intima. This simulation is so close that it even at times undergoes atheroma formation. Furthermore, of immediate concern was the important observation that this type of arterial substitute can and does function successfully for periods well over five years.

The author's results have been outstanding. They have achieved a return of normal circulation in every part of the arterial tree from obstruction in proximal arteries and distal arteries in 80 to 97 per cent of the cases operated upon. In 900 cases of occlusive disease which produced cerebrovascular insufficiency, the circulation was restored in 92 per cent. A relief of symptoms has been maintained in 90 per cent of patients with transient ischemia, in 95 per cent of those with progressive strokes, and in 70 per cent of those with completed strokes. In 300 cases of renal artery occlusive disease associated with hypertension, they achieved successful relief of hypertension in 80 per cent. In 3300 patients with arterial insufficiency of the lower extremities they obtained successful results in 93 per cent with a mortality of 2 per cent.

The classical example of segmental arterial disease is aneurysm in which, in general one encounters normal proximal and distal vascular segments and in which removal and restoration of arterial continuity by patch graft always leads to restoration of a normal circulation. The problems encountered here are more serious than in replacement of, for example, a femoral obstruction, because it is necessary during the operation to arrest the circulation temporarily through the segment to be resected, and this raises the operation risk. Occlusion of the aorta temporarily raises vascular resistance on the heart with left ventricular strain, with at the same time possible ischemic damage to distal tissues. But the cardiopulmonary bypass method with the artificial heart lung machine or a temporary bypass method overcomes the difficulty. In short, technical methods to avoid ischemia and correct obstructions are available for all forms of aneurysm regardless of location and extent. The mortality figures reported by DeBakey are encouraging. In those that survived the operation, a five to ten year follow up study show that the expectancy of life closely parallels a comparable age group in the normal population.

Some extremely important observations on the natural history of atherosclerosis and aneurysms have come out of DeBakeys experimental and clinical studies. One is that the lesions not only may remain localized for long periods of time, but also may stop progressing once the lesion has reached a certain stage. Apparently atherosclerosis tends to progress slowly up to a certain point, beyond which its progression is greatly reduced or even arrested. It is as if atherosclerosis may not be a continuously progressive disease but can be a rather self limited one. The clinical manifestations which appear to be progressive, often are produced by complications of the lesion such as super-imposed thrombosis with consequent ischemic disturbances.

Another feature is the wide variation in the anatomicpathologic features of arteriosclerosis in terms of both mural changes and extent of involvement. In some patients one finds a simple extremely well localized atheroma with no other involvement. In other patients one finds more extensive atheroma formation in multiple sites. In still others the changes are caused predominantly by a process which destroys the media leading to aneurysmal formation. The changes found in atherosclerosis and aneurysm are so different that they suggest a different etiology and a different pathogenesis.

The field is now open for further investigations. We need to know specific etiologies for the different forms of occlusive and aneurysmal disease. It is hoped the need for surgery will wither as knowledge of etiology and resultant preventive measures become available. Then the major cause of death will be conquered and man should reach the natural life span of ninety to one-hundred ten years.

L.H.N.

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Drug Evaluation By The Practitioner

The practicing physician is an important component in drug evaluation. He should not be excluded. Many excellent controlled studies have been performed by well-qualified physicians, who are not members of a medical school or a research facility with a hospital environment. Since the majority of patients treated by a physician are seen in private offices and the majority of drugs introduced into medicine are intended for these patients, it is essential that the evaluation include the practicing physician. Too often the results obtained in a limited group of patients, by competent investigators in scientific institutions, cannot be carried over to the treatment of patients in actual field trials. The so-called controlled studies are occasionally so limited in scope, with removal of random variables, that the final conclusions do not reflect what can be expected when the drug is used in actual practice.—Robert C. Batterman to Western Pharmacology Society, San Francisco, January 28, 1963.

New Drugs And The Practicing Physician

When the physician observes a significant reaction to a drug, he should inform the Council on Drugs of the American Medical Association, which keeps records of untoward reactions and makes reports periodically. He should also inform the manufacturer, who can watch for reports of similar reactions, warn physicians to modify the dose or method of administration, or withdraw the drug from the market if necessary. In addition, the Federal Food and Drug Administration can be notifie since they have the power to remove a toxic drug from the market. In the final analysis, it is the practicing physician who must make the decision whether or not to use a new drug on the particular patient.—Harry F. Dowling, M.D., in *J.A.M.A.*, July 27, 1963

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Clinical Pathology: Progress Report

Roy N. Barnett, M.D., *Guest Editor*

■ Publication of this second number devoted to Laboratory Medicine provides an opportune occasion to bring up to date some of the advances which the organizations of pathologists have made in the years since the excellent review by Dr. Gould[1] in the first Laboratory Medicine issue. This report will not deal with new methodology and techniques, an enormous and exciting field in itself. However none of the technical advances are meaningful without high calibre laboratories in which they can be carried out.

Present Status Of Clinical Laboratory Proficiency

The first step in solving a problem is to identify it accurately. In this field the most reliable index presently available is the analysis of survey results when specimens of known composition are sent to various laboratories for analysis. Although such specimens often receive more careful study than do routine specimens, one can still acquire useful data as to ordinary performance in the laboratories tested. During the last two years the Standards Committee of the College of American Pathologists has made several large scale surveys; including Hemoglobin, Bilirubin, Cholesterol, Prothrombin, Bacteriology, and a Comprehensive Survey which covered Hemoglobin, Differential Blood Count, Blood Group and Rh factor, Urinalysis for specific gravity, protein and glucose, Culture for enteric pathogens, Spinal fluid chloride and protein, and Serum CO_2, Urea Nitrogen, Cholesterol, Na, K and bilirubin. Final reports as to the results of these surveys are currently in preparation and some may have been made public by the time this issue appears.

The conclusions go well beyond the obvious fact that there is great room for improvement, and into such more helpful information as which methods and instruments gave the best results; whether small institutions did as well as larger ones; whether the "Reference Laboratories" of specially interested scientists could all secure identical results; etc. It is easy but fruitless to chastise laboratories for "inaccurate" results; it is far more useful to find out how intrinsically accurate current techniques are, and to then peruse the methods themselves as well as the proper use of these methods.

One preliminary conclusion is the great value of the widespread use of the cyanmethemoglobin standards certified by the College of American Pathologists. Most of the commercial standards now can be purchased with this certification and are used to calibrate hemoglobin curves throughout this country and in several foreign lands. The "spread" of hemoglobin results using this method and these standards is much smaller than was found in earlier surveys using a diversity of methods and calibration techniques. The college has now set up standards for bilirubin and cholesterol which are acceptable to other interested physicians; it is expected that commercially available certified standards will soon be on the market. The bilirubin problem has become a very critical one; if an arbitrary upper limit of 20 mg. is generally accepted for requesting exchange transfusion of newborne infants it is essential that the original pure bilirubin be uniform as well as that methodology be precise.

Another method for evaluation of precision and to a lesser degree accuracy in individual laboratories is the Quality Control program. Now in use in some form in over 800 laboratories in the Eastern United States alone, it requires analysis of serum or similar material of previously determined composition along with the unknown specimens. A Quality Control Manual has been made available to everyone who is interested and is a "must" for all those who perform clinical laboratory analyses. This technique is an excellent check on day to day performance of individual laboratories.

Two new programs are under way. One is the Laboratory Accreditation Program, providing for inspection of all hospital laboratories which desire such inspection. This program provides for necessary education and advice to bring all departments up to standard levels of performance. It should provide essential data to organizations concerned with approving Resident and Interne Training. Another is the Product Evaluation Program. This has been organized to evaluate performance of "kits" for simplified or rapid testing, by comparison with manufacturers' claims. Presently under study are reagent sets for urea, glucose and cholesterol; other procedures will soon be added. It is hoped in this

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way that ultimately even the smallest laboratory will be able to purchase such reagent sets with the assurance that they are reliable within specified limits.

Educational Activities

Two ambitious programs are aimed at postgraduate training of Pathologists and their whole Laboratories. Carried out by the Commission on Continuing Education of the American Society of Clinical Pathologists, these include Film Strips and Check Samples. The Film Strip lectures include colored films and a text narrated by a leading pathologist. For example Dr. Israel Davidsohn discusses the diagnosis of infectious mononucleosis and Dr. Philip Levine recommends good Blood Banking procedures. These are aimed primarily at technologists and student technologists although physicians generally can learn much from them.

The Check Sample Program provides six unknown samples for analysis every year in each of the following fields; Microbiology, Blood Banking, Hematology, Clinical Chemistry, Forensic Pathology and Miscellaneous Fields. Two weeks after the specimen is sent there is a magnificent critique of methodology and interpretation by a selected expert. The opportunity this affords for first finding out how good current performance is and for then making necessary improvements is obvious.

Pathology Residents more and more receive two full years of Clinical Pathology training as well as two years of Pathologic Anatomy. These younger specialists are far better equipped to handle the service responsibilities for patient care than many of their seniors who were taught that the clinical laboratories were an inferior sneered-at branch of medicine, important mainly because they took away valuable time which preferably should have been devoted to autopsies.

Training of technologists and laboratory assistants is also getting needed attention. Without good laboratory personnel the standards of performance cannot be raised. The National Committee for Careers in Medical Technology (NCCMT), sponsored by pathologists and health organizations, has succeeded into interesting many more young people in this dynamic field. Upgrading of educational requirements to a total of four years after high school was achieved in 1961 with only minor dislocations; the Registered Medical Technologist (MT-ASCP) is today on a par in college and employment potentials with other students majoring in biology, chemistry or related fields. Cytotechnologists, requiring two years of college before training in cytology, also attend approved schools and qualify for a national examination. A new program for certified laboratory assistants make available opportunities for high school graduates to spend one year in hospital schools and to receive recognition of their training.

Prospective Programs

There are a few additional goals which are being mulled over for early action.

One goal is an increase in the number of Pathologists and of Ph.D. workers in clinical fields. The volume of work in clinical laboratories is growing out of all proportion to patient-days of medical and hospital care. In hospitals alone many more pathologists could be used profitably at present, and even more will be needed in a few years. The Ph.D., so often confined to academic surroundings, has much to contribute by special knowledge and skills to patient care. This is particularly true in the fields of Biochemistry and Microbiology.

A second and very different goal is the establishment of suitable normal values. This must be correlated with age, sex and geographic location for every commonly used test. Equally important is the following of normal persons over long periods of time. If periodic health checkups come to include basic laboratory analyses we must know what deviations indicate incipient disease, and what deviations are unimportant. Strange as it seems, our information in this field is at present extremely meagre.

Summary And Conclusions

Progress in Laboratory Medicine on the basis of participation by pathologist organizations is presented. Important programs are under way in laboratory evaluation improvement of practice and continuing education of pathologists and laboratory personnel.

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Laboratory Methods In The Diagnostic Evaluation Of Hypertension

Robert J. Levine, M.D.

■ In recent years there have been significant pharmacologic and surgical advances in the management of hypertensive vascular disease. The importance of precise diagnostic evaluation of the patient with hypertension has increased correspondingly. One important objective is to find patients in whom the disease is potentially curable by a surgical procedure. In other patients the information obtained by diagnostic studies may be applied to the rational selection of a course of treatment and to the estimation of the progress and the prognosis of the disease.

The purpose of this paper is to outline a practicable approach to the selection of various laboratory tests for the diagnostic evaluation of the patient with hypertension. It should be understood at the outset that there is not universal agreement on the criteria of selection of patients for special diagnostic studies or on the selection of satisfactory tests for screening and diagnostic purposes. Variations in opinion on these matters have been occasioned by the frequent introduction of new techniques and by the acquisition of increasing experience with older techniques.

General Considerations

The organs which are likely to sustain the greatest damage in hypertensive vascular disease are the kidneys, heart and brain. Therefore, it is of value to ascertain routinely their functional state. Recommended tests for the study of the kidney function are urinalysis, blood urea nitrogen, creatinine clearance, phenolsulfonphthalein (PSP) excretion and intravenous pyelogram (IVP). The urinalysis done on a fresh specimen, should include a measurement of osmolality (or specific gravity), a qualitative test for protein, and an examination of the sediment. If white cells are present, a culture of the urine will often prove fruitful. The IVP may disclose evidence of adrenal tumors, of structural renal disease, or of occlusive renal vascular disease. A suggestion for the modification of the usual IVP technique to make it a more sensitive screening test for unilateral renal vascular disease is discussed below.

Laboratory aids to the evaluation of the heart should include a chest roentgenogram and an electrocardiogram. No routine laboratory test of central nervous system function is likely to add to the information obtained by a complete neurologic examination including careful observation of the ocular fundi. Other tests which are often of value include the complete blood count, the blood sugar, and the serum sodium, potassium, chloride and carbon dioxide.

In the search for specific causes of hypertension sufficient clinical and laboratory observations should be made to rule out such diseases as aortic coarctation, adrenal cortical hyperfunction, collagen vascular disease, polycythemia, drug intoxication (e.g., ergot) and primary central nervous system disease (tumors and encephalitis). There are three causes of potentially curable hypertension which may present an obscure clinical picture and which therefore merit more detailed consideration. These are: occlusive renal vascular disease, pheochromocytoma and primary aldosteronism.

Occlusive Renal Vascular Disease

For the purpose of this discussion, occlusive renal vascular disease may be defined as obstruction of a major renal artery of sufficient severity to result in ischemia of the kidney. If infarction is produced, it is segmental in nature and does not involve the entire organ. Renal arterial obstruction may be caused by a variety of disease processes. Some of the more common of these include atherosclerosis, thrombosis, embolism, aortic dissection, congenital vascular malformations and extrinsic masses which may compress the vessel directly or cause torsion of the renal pedicle. Among currently recognized causes of hypertension which are potentially curable by surgery, occlusive renal vascular disease is, by far, the most common. The problems encoun-

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tered in the diagnosis of occlusive renal vascular disease are the subject of a recent critical review by Howard and Connor[1].

Because the tests required for the diagnosis of occlusive renal vascular disease may be associated with certain hazards to the health of the patient, and because they are both time-consuming and expensive, it is necessary to establish criteria for the selection of patients for these studies. The following criteria for selection are suggested:

1. Historical features: A recent history of pain in the abdomen or in the renal area or unexplained hematuria is suggestive, particularly if the episode was followed by the onset of hypertension or the accentuation of previously mild hypertension. Sudden acceleration of previously mild hypertension is always cause to suspect that significant occlusive renal vascular disease has supervened. The family history seldom contributes to the selection process.

2. The hypertension should be at least moderately severe. The observation of the response to bed rest or sedation is of little value.

3. Unexplained hypertension in a patient below the age of 35.

4. The presence of a systolic or continuous bruit over the renal areas.

5. The absence of evidence of other severe disease or of advanced complications of hypertensive vascular disease involving the heart, brain or kidneys. Nothing is gained by establishing the diagnosis of renal vascular disease in a patient who is too severely ill to undergo surgical treatment. The presence of uremia of mild to moderate degree does not, of itself, preclude the possibility of finding surgically approachable renal vascular disease. The danger of complications of diagnostic studies is increased in patients with renal functional impairment. However, selected patients who meet other criteria may be subjected to these studies, particularly if the renal function improves appreciably as the blood pressure is lowered pharmacologically.

6. The demonstration by IVP of a disparity of greater than one cm. in the length of the kidneys, or of evidence of segmental infarction, or of a difference in the concentration of dye in one kidney as compared with the other. With regard to the variations of concentration of dye in the two kidneys, there are at least two possibilities. Renal arterial obstruction may be so severe that the amount of dye delivered to the involved kidney may be decreased to the point that there is little or no visualization of that kidney. On the other hand, one of the characteristics of an ischemic kidney is that it reabsorbs more water from the tubules than does the normal one. This results in an increased solute concentration within the kidney tubule. Therefore, in some cases the dye may appear earlier and persist longer in the involved kidney than in the uninvolved one. In order to enhance the sensitivity of the IVP in detecting subtle variations in the concentration of dye it is suggested that the usual procedure be altered as follows. The first film should follow the dye injection by only one and two minutes, and the last film by one hour.

The radioisotope renogram has been introduced recently for the purpose of comparing the relative blood flow to each kidney.[2] This is accomplished by scanning the radioactivity over each kidney following the intravenous administration of a dye which has been labeled with a radioactive isotope. This method is safe and, in expert hands, is sufficiently sensitive to serve as a screening test.

Patients who meets one or more of the criteria stated above, and who are not disqualified on the basis of criterion number five, are candidates for aortography for the purpose of visualization of the renal arteries. The techniques of aortography have been reviewed recently by Kincaid and Davis.[3] The most satisfactory results are obtained when the dye is injected directly into the aorta by the transfemoral or by the translumbar route.

The demonstration by aortography of an obstructing lesion in a major renal artery does not necessarily indicate that this lesion is the cause of the hypertension or that the surgical relief of such a lesion will benefit the patient. The degree of renal ischemia and consequent functional alteration may not be significant. Occasionally, partial obstruction of a renal artery in a patient with essential hypertension actually will protect the kidney from the effects of the high blood pressure and preserve its function. The consequences of nephrectomy or of attempted vascular reconstruction in such cases may be disastrous. Therefore, if an obstructing lesion is demonstrated in a major renal artery, it becomes necessary to study the function of each kidney independently by means of simultaneous ureteral catheterization (Howard test). The preferred technique for this procedure and its interpretation have been described by Stamey, et al.[4]

Pheochromocytoma

Pheochromocytomas are rare tumors which arise in the adrenal medulla or in sympathetic nervous tissue and which produce hypertension by the secretion of large quantities of catectolamines (norepinephrine and epinephrine). In each hypertensive patient at least one test should be undertaken to explore the possibility of the existence of such a tumor. Certain clinical features may be present which make it necessary to pursue the diagnosis further, even though the first screening test may have yielded a negative result. There may be a family history of pheochromocytoma. There may be evidence in the patient or in his family of neurofibromatosis or of angiomata of the retina or cerebellum. The patient may experience paroxysmal episodes of any or all of the following: hypertension, headache, palpitation, tachycardia, dizziness, sweating, or cutaneous blanching or flushing. Other suggestive clinical features include marked postural hypotension and evidence of hypermetabolism, impaired glucose tolerance, and increased hematocrit. The increased hematocrit may represent a true increase in blood volume or a decrease in plasma volume (stress polycythemia). An abdominal mass may be present, the massage of which may precipitate a typical paroxysm. There may be roentgenographic evidence of a tumor mass in the chest or in the abdomen.

The preferred tests for the diagnosis of pheochromocytoma are quantitative assays of the urinary excretion of catecholamines or their metabolites, vanilmandelic acid (VMA) or the methylated metabolites metanephrine and normetanephrine. Since a detailed consideration of the relative merit of the various available procedures is beyond the scope of this discussion, the reader is referred to recent reviews of this subject.[5, 6] Because of its relative simplicity, the assay of urinary VMA is made available most commonly in clinical chemistry laboratories. It is somewhat less sensitive than the assay for catecholamines. Therefore, if strong clinical suspicion persists even after the VMA excretion has been found to be normal, it is worthwhile to assay urinary catecholamine excretion. Any positive results obtained by semiquantitative or so-called "rapid screening techniques" should be confirmed by quantitative assays before the diagnosis is considered established.

The usefulness of pharmacologic screening procedures such as the intravenous injection of phentolamine (Regitine (R)) or histamine has become quite limited. Chemical techniques are preferred since they are more reliable and they entail no hazard or discomfort. However, in some situations the pharmacologic tests may provide valuable information which is not otherwise obtainable. During a period when the pheochromocytoma is not releasing pressor substances into the blood, the patient's blood pressure may be normal and the urine may contain normal amounts of catecholamines and metabolites. At such times, the rapid intravenous injection of histamine (dose 0.010 to 0.025 mg.) may result in a rapid rise in blood pressure. The specificity of this reaction may be enhanced greatly by the demonstration of a corresponding increase in the blood or urinary levels of catecholamines. In a patient who is severely ill due to hypertension it may be necessary to institute specific treatment before specimens for chemical determinations can be obtained. At such times it is useful to observe the effect of the rapid intravenous injection of phentolamine (dose 5 mg.) on the blood pressure. A sharp decrease is suggestive of a pheochromocytoma. It should be noted that these tests may produce dangerous effects when positive. Therefore, suitable antidotes for each drug should be readily available; phentolamine for the histamine test and norepinephrine for the phentolamine test. For a detailed account of the techniques and interpretations of these pharmacologic tests the reader is referred to reference number 7.

Primary Aldosteronism

Primary aldosteronism is the term applied to the rare syndrome which results from the excessive production of aldosterone by a tumor of the adrenal cortex or, even more rarely, by a hyperplastic adrenal cortex. Typical clinical features of this syndrome include weakness which may be constant or episodic, tetany, polyuria, polydipsia, paresthesias and headache. Hypertension is usually mild to moderate except in certain cases which begin during childhood in which there may be malignant hypertension. Edema is usually absent. Characteristic laboratory findings include hypokalemia, hypernatremia, metabolic alkalosis, and neutral or alkaline urine of low concentration. In patients who present the typical clinical syndrome the diagnosis is established by the measurement of increased urinary aldosterone levels. In some cases in which urinary aldosterone levels are normal, the aldosterone secretory rate may be found elevated by a more complex but more sensitive method.

The relationship between aldosterone and hypertension is the subject of a recent review by Conn,[8] who first described primary aldosteronism in 1955. In hypertensive patients, increased aldosterone secretion in the absence of an adrenal cortical tumor (secondary aldosteronism) may be associated with severe or malignant hypertension, occlusive renal vascular disease, low sodium intake, or uremia. Thus, the problem in diagnosis lies in distinguishing between primary and secondary aldosteronism. A number of physiologic approaches to this differential diagnosis have been proposed, none of which appear to offer consistent and specific results.[8, 9]

One useful screening test for aldosteronism consists of the determination of the ratio of sodium to potassium in the saliva.[10] A decreased ratio is found in patients with excessive aldosterone secretion. The procedure is simple and inexpensive but, unfortunately, does not distinguish between primary and secondary aldosteronism.

In some cases the final diagnostic procedure must be exploratory surgery. The decision to explore the patient for an aldostrone-producing tumor is favored by the following observations:

1. Characteristic features of the syndrome of primary aldosteronism as listed above.

2. Persistent hypokalemia in the absence of diuretic therapy. It is often difficult to restore the serum levels to normal even with the administration of large amounts of potassium.

3. The presence of high urinary levels of potassium (greater than 20 milliequivalents per liter) at a time when the serum level and daily intake of potassium are low.

4. The ability to restore serum potassium values to normal by treatment with spirolactone (Aldactone (R)) . A failure in this regard indicates that the hypokalemia is due to something other than excessive aldosterone (e.g., potassium-wasting nephritis).

5. High plasma volume. Plasma volume is usually not elevated in secondary aldosteronism.

6. Hypernatremia. Hyponatremia is more likely to be found in secondary aldosteronism.[8]

7. Evidence of a supra-renal mass on IVP. This is rarely found, since these tumors are usually quite small. Laminograms of the renal area may augment the sensitivity of the IVP for the purpose of demonstrating adrenal tumors.

8. The possibility of occlusive renal vascular disease must be excluded by aortography.

Comment

It is often necessary to rely heavily upon the results of laboratory determinations in the diagnostic evaluation of the hypertensive patient. Therefore, it is extremely important that these tests be done under conditions which will ensure their accuracy and reliability. One must be on guard against drug-induced technical artifacts or physiologic alterations which may lead to erroneous conclusions. For example, many of the laboratory manifestations and even some of the clinical features of primary aldosteronism may be induced artificially by the administration of thiazide diuretics. Also, the significance of the values obtained by assays of catecholamines and their metabolites may be altered greatly during treatment with several drugs including certain antibiotics and expectorants, sympathetic amines, and drugs which inhibit monoamine oxidase or decarboxylase activity. Prior to collection of specimens the physician is urged to contact the laboratory to find out the required technique for the collection of specimens and the drugs to be avoided during the period of collection.

Summary

This paper outlined an approach to the selection of laboratory methods to aid in the diagnostic evaluation of the patient with hypertension. Particular attention was devoted to methods of diagnosis of diseases which are potentially curable by surgical procedures. Also discussed were general approaches to the estimation of the extent of involvement, the rate of progress and the response to therapy of patients with hypertensive vascular disease.

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A Simple, Rapid Microicterus Test For Estimating The Degree Of Jaundice

Raymond L. Casella, M.D. and Sam J. Piliero, Ph.D.

Introduction

■ A simple, rapid, reproducible test has been developed which will be of assistance to those who have frequently encountered difficulties in estimating the degree of jaundice in newborn infants and certain adults with liver disease. This method will possibly overcome some of the shortcomings inherent in the interpretation of skin changes in these situations.

A preliminary report has been published elsewhere.[1]

Materials And Methods

Microicterus standards were established by preparing serial dilutions of potassium dichromate (C.P.) as for the icterus index procedure of Kolmer.[2] Briefly, this consists of a 1 per cent aqueous solution of dichromate acidified with two drops of concentrated sulphuric acid. Volumes of the standard solution were pipetted into test tubes according to the following scheme: 10.0 ml., 5.0 ml., 3.0 ml., 2.0 ml., 1.5 ml., 1.2 ml., 1.0 ml., 0.7 ml., 0.5 ml., 0.3 ml., and 0.1 ml. All tubes were brought to a final volume of 10.0 ml. with distilled water. The dilutions were transferred to standardized microhematocrit tubes and both ends carefully sealed, (Figure I).

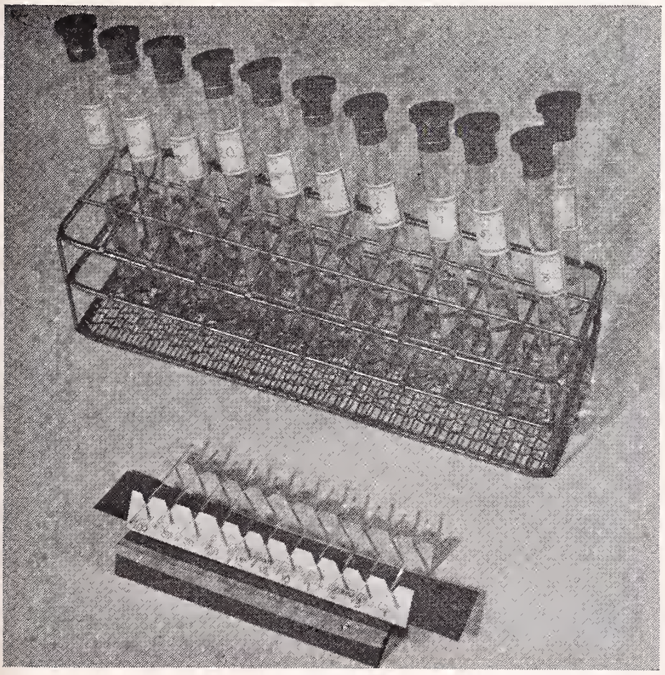

Figure I
Microicterus standards.

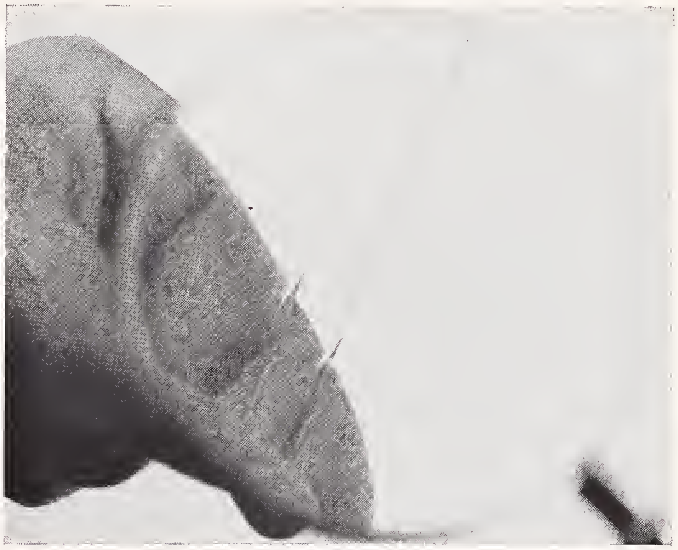

Figure II
Visual comparison of standard tube with tube containing the patient's plasma.

A reader was prepared by arranging the sealed tubes in a serial order of decreasing concentrations.

The experimental plan was established as follows:

Group A. Peripheral blood was obtained from fifty adult patients selected at random from the medical wards. In four cases, it was possible to obtain serial readings. All blood was drawn from the finger tip, directly into microhematocrit tubes and spun at 12,000 RPM for seven minutes. With the aid of a hand lens, the microicterus (M.I.) values were determined by visual comparison of the standard tubes with the tubes containing the patient's plasma, (Figure II).

Simultaneously, serum bilirubin determinations were made by the method of Malloy and Evelyn.[3]

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Readings were made as recommended by Ducci and Watson.[4]

Group B. Peripheral blood samples were obtained from eight infants selected at random from the nursery and subjected to the same procedures as in Group A.

The values of the M.I. and of the serum bilirubin for both groups were recorded along with the clinical visual estimation of jaundice.

A graduated scale was established correlating the microicterus value (M.I.), degree of visible jaundice and serum bilirubin values.

Results

The adult M.I. scale (Figure III) indicates that M.I. values of 1 to 7 are normal in terms of normal serum bilirubin values and visible jaundice. Values ranging from 10-20 M.I. correlate well with increasing levels of serum bilirubin. The lack of visual jaundice over this range is not reflected in either the M.I. or serum bilirubin values. M.I. values exceeding 20 are consistent with elevated serum bilirubin and the presence of visible jaundice.

Table I shows that twenty-four per cent of the group studied exhibited visible jaundice which was accompanied by high M.I. values (20-100) and an increasing total serum bilirubin concentration (4-47.3 mg. per cent). In only one patient a high serum bilirubin (4.6 mg. per cent) was detected without visible jaundice and a low level M.I. (3). Noteworthy also is the observation that only a single patient with no visible jaundice revealed a M.I. value in the lower segment of the upper range (20) and an elevated serum bilirubin value of 3.6 mg. per cent.

From serial studies (Table II) a clear correlation between increasing M.I. and total serum bilirubin concentrations is observed in patients I, III, and IV. Moreover, patient IV, examined during the clinical stages of no visible jaundice, jaundice and fading jaundice, exhibited consistent agreement with the M.I. scale

The proposed infant M.I. scale is indicated in Figure IV and reveals that M.I. readings of 1 to 7 are considered normal. Table III demonstrates that a value of 20 represents an increasing serum bilirubin level to 4.0 mg. per cent, with no skin jaundice, while a value of 30 is observed in a case of questionable skin jaundice with a total serum bilirubin value of 5.3 mg. per cent. An M.I. value of 50 with a total serum bilirubin content of 9.8 mg. per cent

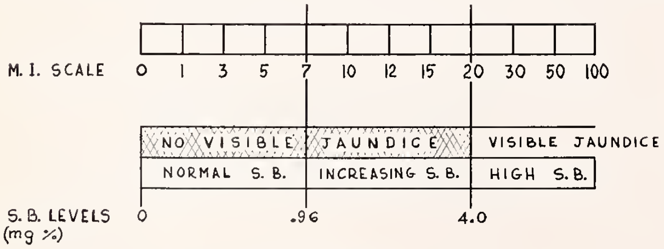

Figure III
The adult microicterometer scale.

Table I
Adult Determinations

CASE NO.	SEX	AGE	VISIBLE JAUNDICE	M.I.	HCT PER CENT	SERUM TOTAL	BILI- RUBIN DIRECT	MGM % INDI- RECT
1	F	27	+	50	45	17.5	16.2	1.3
2	F	34	+	30	39	5.5	5.5	0.5
3	M	23	0	15	43	2.1	1.3	0.8
4	M	31	0	12	36	1.6	0.4	1.2
5	M	28	+	50	45	16.7	15.3	1.2
6	M	23	+	20	43	4.0	3.4	0.6
7	M	36	0	10	30	3.3	1.8	1.5
8	F	67	0	3	28	0.8	0.48	0.3
9	F	55	0	3	45	0.3	0.08	0.25
10	F	55	+	50	36	13.5	12.4	1.1
11	M	23	0	10	46	1.8	1.3	0.5
12	M	40	0	12	23	2.9	2.6	0.3
13	M	22	0	12	52	1.8	1.1	0.7
14	F	24	0	3	26	0.9	0.9	0.0
16	M	22	0	12	44	1.6	0.6	0.96
17	F	55	+	100	33	18.4	17.6	0.8
18	F	27	0	5	37	1.2	1.2	0.0
19	M	69	0	7	33	2.0	2.0	0.0
20	M	23	+	100	39	47.3	44.4	2.9
21	M	28	+	100	41	20.9	20.9	0.0
22	M	68	0	10	28	2.7	2.1	0.6
23	M	36	0	7	30	0.96	0.96	0.0
24	F	58	0	3	36	0.16	0.16	0.0
25	M	50	0	5	41	1.5	0.96	0.54
26	M	49	0	5	42	0.34	0.16	0.18
27	M	62	0	7	40	1.5	0.40	1.1
28	M	27	0	5	27	0.6	0.23	0.45
29	M	77	0	5	25	0.92	0.62	0.28
30	F	9	0	3	29	0.16	0.16	0.0
31	F	21	+	50	36	13.5	11.3	2.2
32	F	58	+	50	27	9.6	6.3	3.3
33	F	86	0	3	19	0.69	0.08	0.61
34	F	19	0	20	37	3.6	3.0	0.6
35	F	23	0	3	28	0.57	0.0	0.57
36	F	32	0	3	20	0.15	0.14	0.01
37	M	48	0	7	41	0.57	0.08	0.49
38	M	66	0	3	38	4.6	0.0	4.6
39	M	53	0	5	27	0.48	0.48	0.0
40	F	57	0	12	34	1.5	0.88	0.62
41	F	67	0	3	29	0.69	0.08	0.61
42	F	32	0	3	32	0.46	0.0	0.46
43	F	52	0	3	30	0.11	0.0	0.11
44	F	23	0	3	28	0.16	0.16	0.0
45	M	19	0	12	34	1.5	0.16	1.3
46	M	22	+	100	39	27.2	19.6	7.6
47	M	42	0	3	32	0.16	0.16	0.0
48	F	35	0	15	40	3.5	3.5	0.0
49	M	41	0	3	30	0.46	0.08	0.38
50	M	50	0	12	36	1.5	0.24	1.26

Table II

Adult Serial Determinations

CASE NO.		SEX	AGE	VISIBLE JAUNDICE	M.I.	HCT. (%)	SERUM TOTAL	BILIRUBIN DIRECT	(MGM %) INDIRECT
1.	Initial	M	28	+	50	45	16.7	15.3	1.2
	5 days later			+	100	41	20.9	20.9	0.0
2.	Initial	M	36	0	10	30	3.3	1.8	1.5
	5 days later			0	7	30	0.96	0.96	0.0
3.	Initial	F	55	+	50	36	13.5	12.4	1.1
	5 days later			+	100	33	18.4	17.6	0.8
4.	Initial	M	22	0	12	52	1.8	1.1	0.7
	12 days later			+	100	39	27.2	19.6	7.6
	21 days later			0	12	44	1.6	0.6	1.0

is seen in a case that represents trace skin jaundice. In five infants, M.I. values of 100 with serum bilirubin levels from 10.3-14.4 mg. per cent are observed where skin jaundice is evident.

Discussion

A simple method of detecting, evaluating and following the degree of jaundice in certain adult patients with liver disease and in newborn infants has been described.

As indicated in the results, there is a lack of visual jaundice, in patients with M.I. values from 10-20 correlated with increasing levels of serum bilirubin (0.96-4.6 mg. per cent). As mentioned by Miller,[5] this can be explained by the fact that higher values of serum bilirubin are required before jaundice becomes clinically evident in adults and is attributable to the affinity of elastic tissue for bilirubin. In similar fashion, the differences noted when comparing the adult and infant scales may be reconciled when we consider that the elastic tissues of infants and children are still poorly developed. Therefore, as demonstrated by our findings, serum bilirubin values must reach still higher levels before jaundice is detectable in the infant.

Analysis of simultaneously determined values of serum bilirubin and M.I. in the same patient (adult or infant), revealed that these values tend to parallel each other. However, it should be pointed out that the value of either one is not directly predictable from the known value of the other.

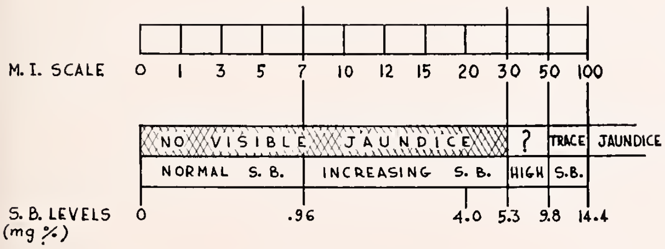

Figure IV

Proposed infant microicterometer scale.

Some of the advantages of the described microicterometric method are as follows:

1. Eliminates the necessity of drawing large samples of blood by venous methods, a factor which is especially desirable in newborn infants.
2. Can be performed simultaneously with the hematocrit determination on every patient, (which is becoming a routine hospital procedure) as a recorded value and point of reference.
3. Results are immediately available and can be repeated as often as necessary.
4. Eliminates the need of requesting special tests in following a serial study of jaundice, or for early detection of jaundice.
5. Indicates what cases should have a special test (serum bilirubin) for greater accuracy when the M.I. determination reveals a high level.
6. In adult cases of jaundice, serial tracing of the degree of jaundice can be performed to determine the daily prognosis and drug effectiveness.

Summary

A method has been described which simplifies the search for early jaundice in the nursery and

Table III

Infant Determinations

CASE NO.	SEX	AGE	VISIBLE JAUNDICE	M.I.	HCT. (%)	SERUM TOTAL	BILIRUBIN DIRECT	(MGM %) INDIRECT
1	M	36 hrs.	+	100	60	13.0	0.7	12.3
2	M	37 hrs.	+	100	65	11.2	0.8	10.4
3	F	5 days	+	100	58	14.4	2.0	12.4
4	F	24 hrs.	+	100	60	12.6	0.4	12.2
5	F	24 hrs.	+	100	58	10.3	0.35	9.95
6	M	72 hrs.	0	20	49	4.0	0.3	3.7
7	M	9 hrs.	?	30	52	5.3	0.3	5.0
8	M	15 hrs.	trace	50	43	9.8	0.8	9.0

elsewhere, without the use of expensive special equipment. The value of the microicterometer lies in its availability, speed, micro-blood sample requirement and ease of determination. Some of the uses of the method are as follows:

A. The establishment of a reference point in detecting the presence of early jaundice especially at the time of birth.

B. In tracing the degree of jaundice in babies over a period of hours or days.

C. As a screening procedure for use in blood banking centers.

Acknowledgements

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Discovery

Whether or not it is true that the age of the adventurer in the physical world is now closed, adventure in the world of thought is still open to every soul that is not wholly tamed and in love with the cage. It has always been more difficult than adventure in the ordinary sense, and it is becoming more difficult every day. Uniformity of thought is increasingly the apparent goal and demand of civilization; education has no use for the fires of rebellion, and even science itself is not above lending an occasional hand at the fire-engine. Still there burns on in most of us a small wild spark. I advise you to nourish it as a precious possession. Do not, however, be under any misapprehension. Really to think for oneself is as strange, difficult, and dangerous as any adventure, and, as the wise ones say, "it will do you no good"; but, like virtue—which it does not otherwise greatly resemble—it will be its own reward.

—The Collected Papers of Wilfred Trotter, F.R.S.
London, Oxford University Press, 1946, p. 88.

Electron Microscopy In Medical Diagnosis

W. Robert Adams, M.D.

■ The tremendous magnification afforded by the electron microscope (up to one million total magnification) has long given rise to hopes that the instrument could be utilized fruitfully in the diagnosis of disease. This hope has remained largely unrealized until recent times for a number of reasons. The limited penetrating powers of the electron beam have required that the specimen be extremely thin. For the same reason it is required that the specimen be dehydrated and examined in a vacuum. The usefulness of electron microscopy as a diagnostic technique has also been limited by the fact that only a few substances could be profitably used as fixatives and stains. Further complexities were present in the form of stringent requirements for a plastic embedding medium for the specimens to be examined and for specialized techniques for cutting sections no more than a few dozen molecular diameters in thickness. It might be said then that in the early days of electron microscopy staining and fixation of specimens were erratic and unreliable, the cutting of sections was difficult, and the interpretation of the results obtained was fraught with numerous uncertainties.

In spite of these difficulties there have been some attempts to use the electron microscope in the diagnosis of disease. Identification of virus particles from material obtained from skin lesions and from spinal fluid in a human case of herpes zoster was carried out as long ago as 1945 by Evans and Melnick[1]. This was before the advent of the negative staining technique, and it was impossible to make specific or group identification of the virus particles that were isolated. The negative staining technique has recently been used by Smith and Melnick[2] to study the surface structure and nucleic acid content of the following viruses: 1. Herpes; 2. Polyoma virus; 3. Molluscum contagiosum; 4. Vacuolating agent (SV40); 5. Vaccinia; 6. Reovirus; 7. Influenza virus; 8. Human papilloma virus; 9. Bacteriophage T4; 10. Poliovirus type 3.

Through refinement of old techniques and development of new techniques in recent years, many of the difficulties of electron microscopy have been either eliminated or considerably diminished, and many of the techniques reduced to reliable routine. The preparation of high quality electronmicrographs still requires considerable care, effort and expense, and for this reason it seems likely that the most important usage of electron microscopy will remain in the field of basic investigative science for many years to come. There are a few aspects of electron microscopy, however, that would seem to have some limited use in the routine diagnosis of certain diseases, and it is the purpose of the present article to discuss one of the most promising of these new approaches. The technique that I wish to discuss here is the identification of virus particles in body fluids and tissue extracts. This technique is rendered feasible by two unique developments in the field of electron microscopy.

The first of these is the demonstration of the specific structure of the external surface of virus particles by means of the phosphotungstic acid (PTA) negative staining technique. Although the principle of "negative staining" had been discovered as early as 1954 by Farrant,[3] the first comprehensive development of the technique and its rigorous application to the study of the structure of viruses was carried out by Brenner and Horne[4] and Horne and Wildy.[5] The principle is simple in theory. If a relatively electron transparent object (such as a virus particle or protein molecule) be deposited on an electron microscope specimen film and then have applied to it a matrix of electron dense material such as sodium phosphotungstate, the latter will "flow" into any crevices that are to be found on the surface of the particle. Such particles are said to be negatively stained since they are observed in the electron microscope as bright silhouettes against the dark background of the PTA. Strictly speaking then, PTA is not a stain in the usual sense, but merely serves as an "embedding" medium for enhancing contrast. Figures I and II illustrate how this technique may be used to enhance detail and facilitate measurements of a protein molecule. The iron containing protein molecule, ferritin, is shown unstained (Figure I) and stained with PTA (Figure II). Note that in the unstained preparation the protein moiety is invisible, its presence being inferred from the presence of the dense iron hydroxide core, whereas treatment with PTA clearly demonstrates that this protein component is in the form of a spherical shell surrounding the dense core.

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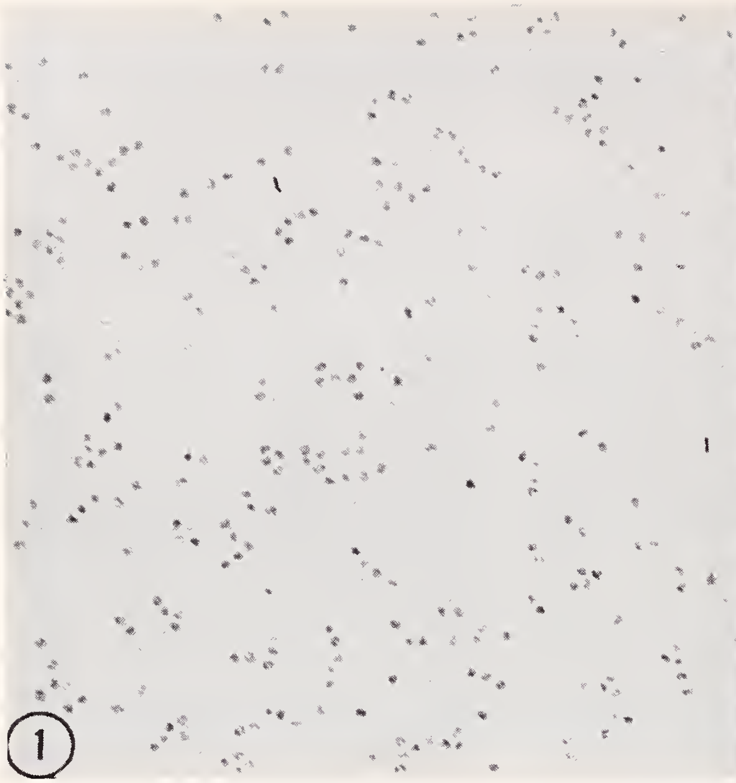


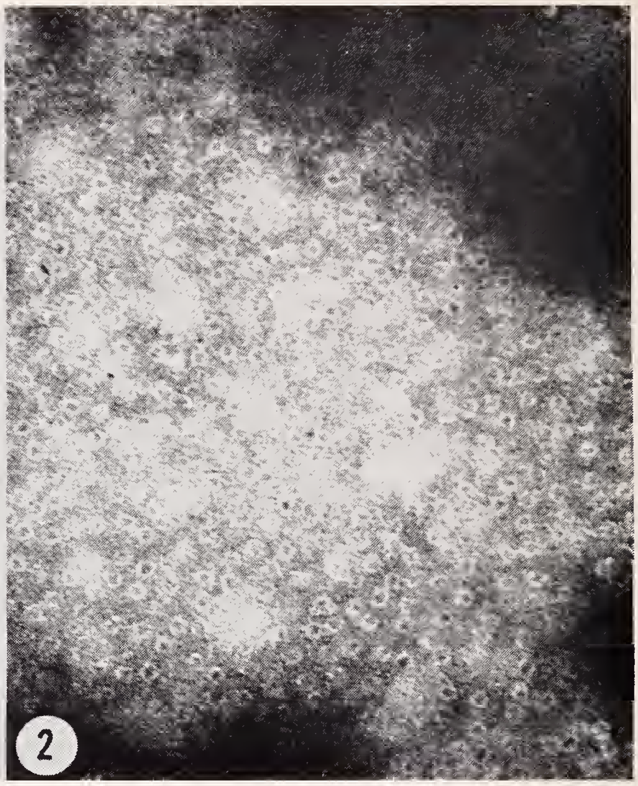


Figure I

Unshadowed, unstained droplet preparation of the iron containing protein molecule, ferritin. The ferric hydroxide core of individual molecules is the only portion of the molecule visible. The protein moiety, invisible in this preparation, is actually in the form of an approximately spherical shell which is readily apparent in the negatively stained preparation illustrated in Figure II. Magnification x 100,000.

Figure II

Ferritin preparation similar to that shown in Figure I but negatively stained with sodium phosphotungstate. In addition to the ferric hydroxide core, seen also in Figure I, the negative contrast provided by the dense phosphotungstate matrix clearly delineates the spherical, relatively transparent protein shell. Magnification x 100,000.

The remarkable crystalline symmetry of the protein coat (capsid) of most viruses demonstrable with the negative staining technique has led Horne and Wildy[5] to propose that this property of the virus particle be used as a morphological basis for virus classification. As is the case in any rapidly developing field there are at present ambiguities in interpretation. For instance, Melnick[6] has recently proposed a capsomere number of 42 for the papova group of viruses and Mayor and Melnick[7] have more recently presented further confirmatory evidence for this proposal. Mattern[8] has recently contested Melnick's proposal, arguing that a capsomere number of 92 is equally consistent with the morphologic data. It can be safely assumed that such uncertainties will be resolved as more precise morphological data are acquired. In any event it is clear that the negative staining procedure has now reached a degree of perfection which allows the group identification of an increasing number of viruses solely on the basis of their surface structure. The outer envelope of the virus particle is referred to as the capsid and the individual macromolecular subunits which constitute the capsid are referred to as capsomeres. The number of capsomeres is related to the icosahedral structure of the virus particle according to equation (1):

$$N = 10x(n-1)^2 + 2 \tag{1}$$

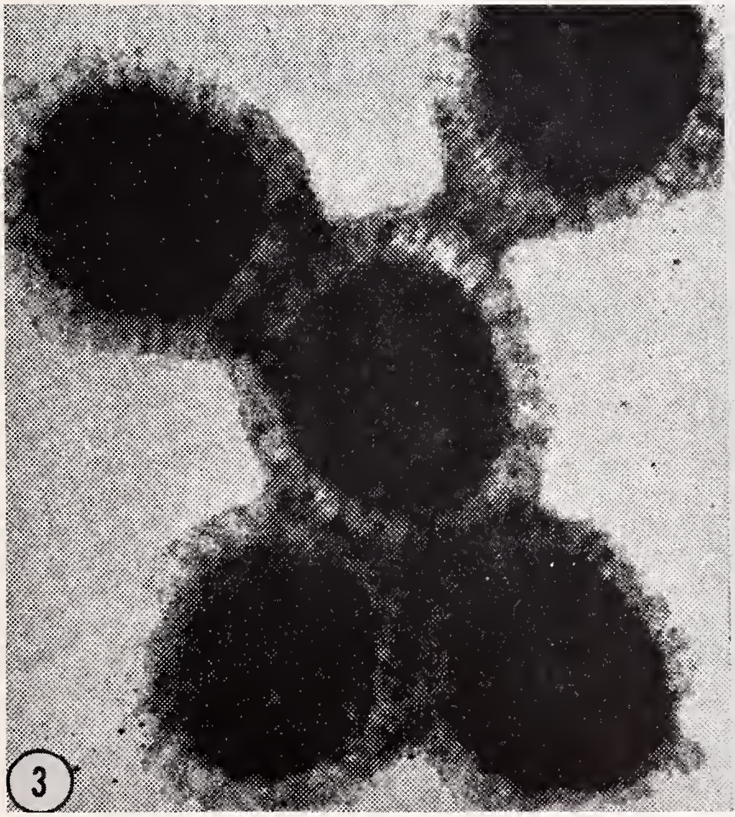
where N = total number of capsomeres, x and n are integers, and n = the number of capsomeres along any one edge of the icosahedron. To date virus capsids have been described where $n = 2,3,4,5,6$, and 10.[7]

An example of the usefulness of this technique is the recent work of Smith and Melnick[9] in the rapid diagnosis of skin lesions suspected to be of viral etiology. Under favorable conditions a presumptive diagnosis can be made within three hours following the obtaining of material from the lesion in question. Figures III and IV are reproduced by permission from their recently published paper[9] and illustrate herpes virus particles stained with uranyl acetate (Figure III) and with potassium phosphotungstate (Figure IV) to delineate the structure of the capsid.

Since capsid structure can be used only as the basis of group identification of virus particles and is not (yet) useful in identifying specific members of a group, it is evident that maximum usefulness of the negative staining method is achieved only when it is used in conjuction with specific immune typing methods. When the two methods are used together, however, considerable time and labor can be saved. In the laboratory of Melnick,[10] for instance, material for routine virus identification is now first screened for group identification using the PTA and/or uranyl acetate methods. Specific identification is then made using immune typing sera. The number of serologic typing procedures is thus reduced approximately 10 fold (from about 300 to a more manageable 20 or 30).

The second important technical development that has added to the usefulness of electron microscopy in several routine situations has been the recent development by Sharp[11,12] of a method for quantitatively examining fluid for the presence of virus particles. In theory the technique is very simple, and in practice the method developed by Dr. Sharp is ingenious. One ml. of the fluid to be examined is placed in a specially designed centrifuge rotor containing an agar block at the bottom of the cell. Centrifugation is then carried out at speeds sufficient to sediment virtually all of the contained virus particles. Following this the agar block is removed and its surface, containing the sedimented virus particles, is covered with a thin film of formvar or collodion which is then stripped away, removing the virus particles with it. The resulting collodion film containing the adhrent virus particles is then treated with any of a number of stains and/or fixatives, the most common being uranyl acetate and lead hydroxide either with or without prior staining with the vapors of osmium tetroxide. The staining and fixation is usually followed by shadowing with a metal such as palladium or chromium. The specimen thus prepared is then inserted in the electron microscope and several random fields photographed. The resulting slides are then projected on a standard counting grid and average counts of the particles tabulated.

Figure V illustrates the typical appearance of such an examination. The virus in this case is Newcastle disease virus. These pictures were taken during the course of an investigation of the ratio of number of virus particles present to the number of plaque forming units (a measure of infectivity). For most viruses this number ranges from 10 to over 1000. The assumption is that the ratio would be 1 if



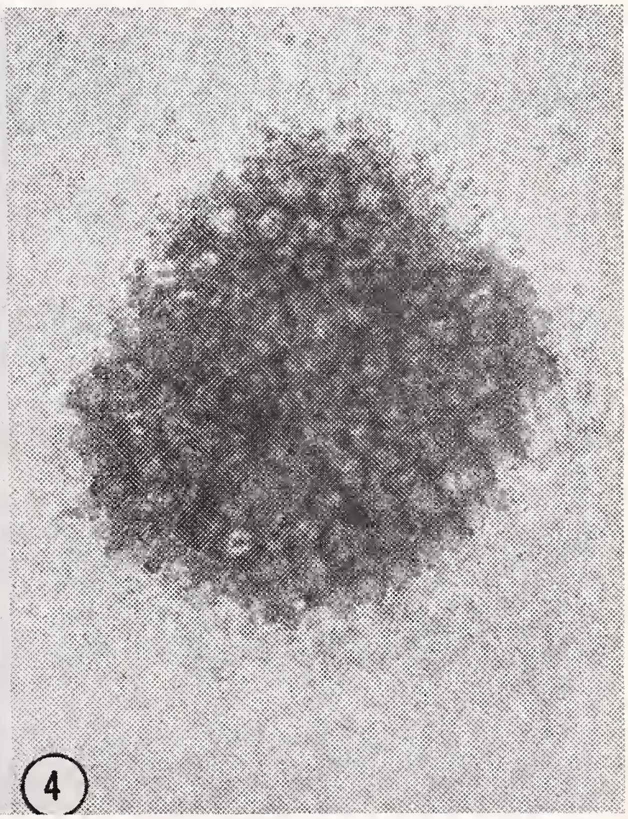
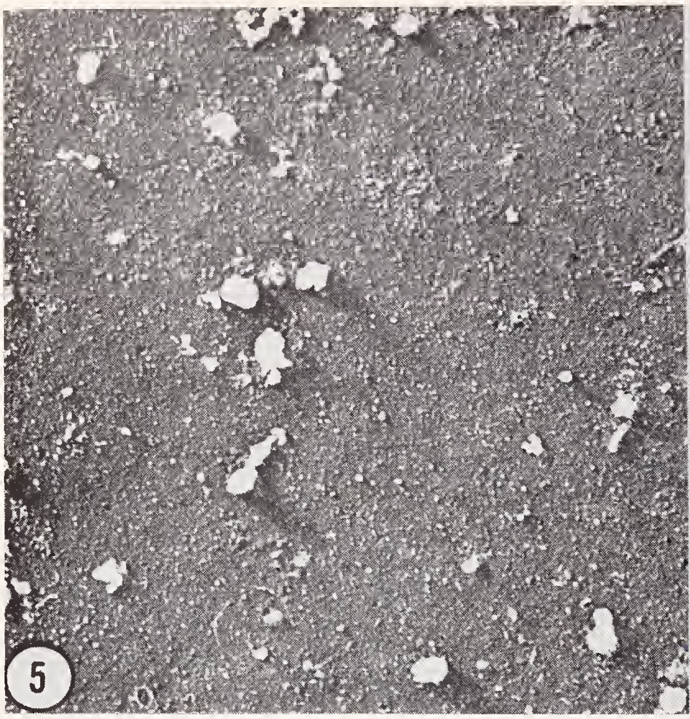


Figure III

Herpes virus particles obtained directly from human vesicular fluid. Group of five virus particles stained with uranyl acetate. Magnification approximately x 350,000. (Reproduced by permission of Dr. Joseph L. Melnick from *Science,* 137: 543.)

Figure IV

Herpes virus particles as in Figure III stained with potassium phosphotungstate at pH 7.0. Individual capsomeres are visible as short, apparently hollow structures probably cylindrical in shape. Magnification approximately x 350,000. (Reproduced by permission of Dr. Joseph L. Melnick from *Science,* 137: 543.)



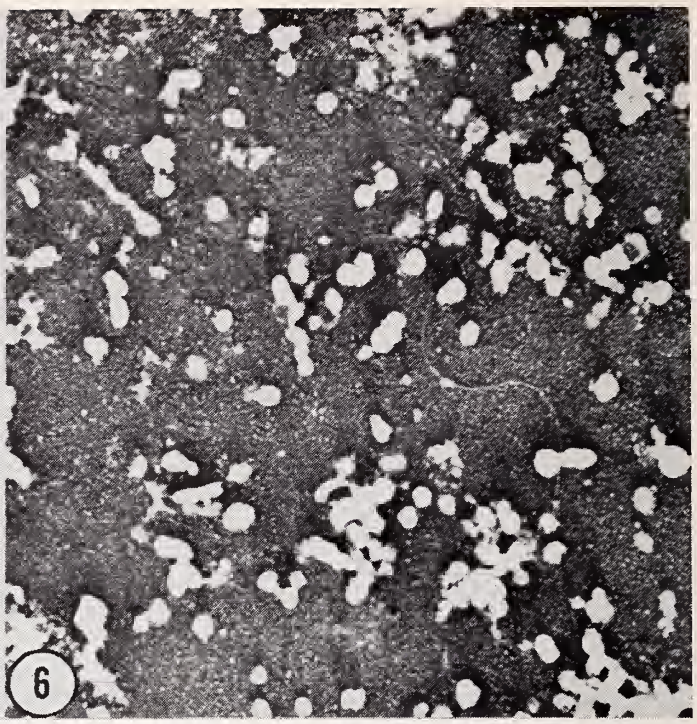


Figure V

Newcastle disease virus particles prepared by the Sharp particle counting technique by sedimentation on agar, stained with 1 per cent uranyl acetate and shadowed with chromium. Particle concentration in the sample examined was approximately 10^8 particles/ml. Magnification x 10,000.

Figure VI

Particles isolated by the Sharp particle counting technique from the serum of a patient with serum hepatitis. Stained with uranyl acetate and shadowed with chromium. The particles vary in diameter from 150 $m\mu$ to 400 $m\mu$. Considerable artifactual flattening is evident. Positive identification of these particles has not been made. Magnification x 10,000.

conditions were ideal; however, excessive sensitivity of the parameter of infectivity yields the practical result that in almost all cases examined so far the ratio has been considerably greater than 1. In the present experiment the number of particles present per ml. of fluid was in the neighborhood of 3.3×10^{11} while the infectivity titer was approximately 1.9×10^{10} yielding a ratio of counted particles to infective units of 17.

An example of how this technique may be used in the study of tissue fluids suspected of containing virus particles is illustrated in Figure VI. This illustration represents a typical photograph of a serum specimen purified by density gradient centrifugation from a patient with infectious hepatitis. This photograph is part of a series of experiments currently being carried out by Dr. Alfred M. Prince and the author in a search for the virus of serum hepatitis. Because of dilution problems and the presence of similar but nonspecific particles within most normal sera it is difficult at the present time to accurately count virus particles in sera or tissue fluids if the particle concentration is less than 10^9 particles per ml.

Figure VII is an electron micrograph of a field similar to that shown in Figure VI but at somewhat greater magnification and indicating both internal and surface structure. The size of the particle has not yet been accurately determined. Although most particles measure more than 200 $m\mu$ in diameter in this and similar photographs, it must be remembered that this is after prolonged centrifugation and treatment with a number of agents. As a result it is only to be expected that the electron micrographs reveal considerable distortion of both shape and size of the particles. Flattening, leading to increase in apparent diameter, is the most severe artifact. Although the virus-like particles here demonstrated were seen in serum samples from a patient with serum hepatitis it must be emphasized that the identification of these particles as the virus of serum hepatitis remains no more than presumptive. A number of unsettled questions remain before a definitive interpretation can be given. One of the first and most important of these unresolved questions relates to the "fingerprint" or capsid structure of the virus of serum hepatitis.

Although the chief utility of electron microscopy would still appear to remain within the field of basic investigative morphology and development of new and rapid techniques for examination of tissues and fluids would appear to pave the way for

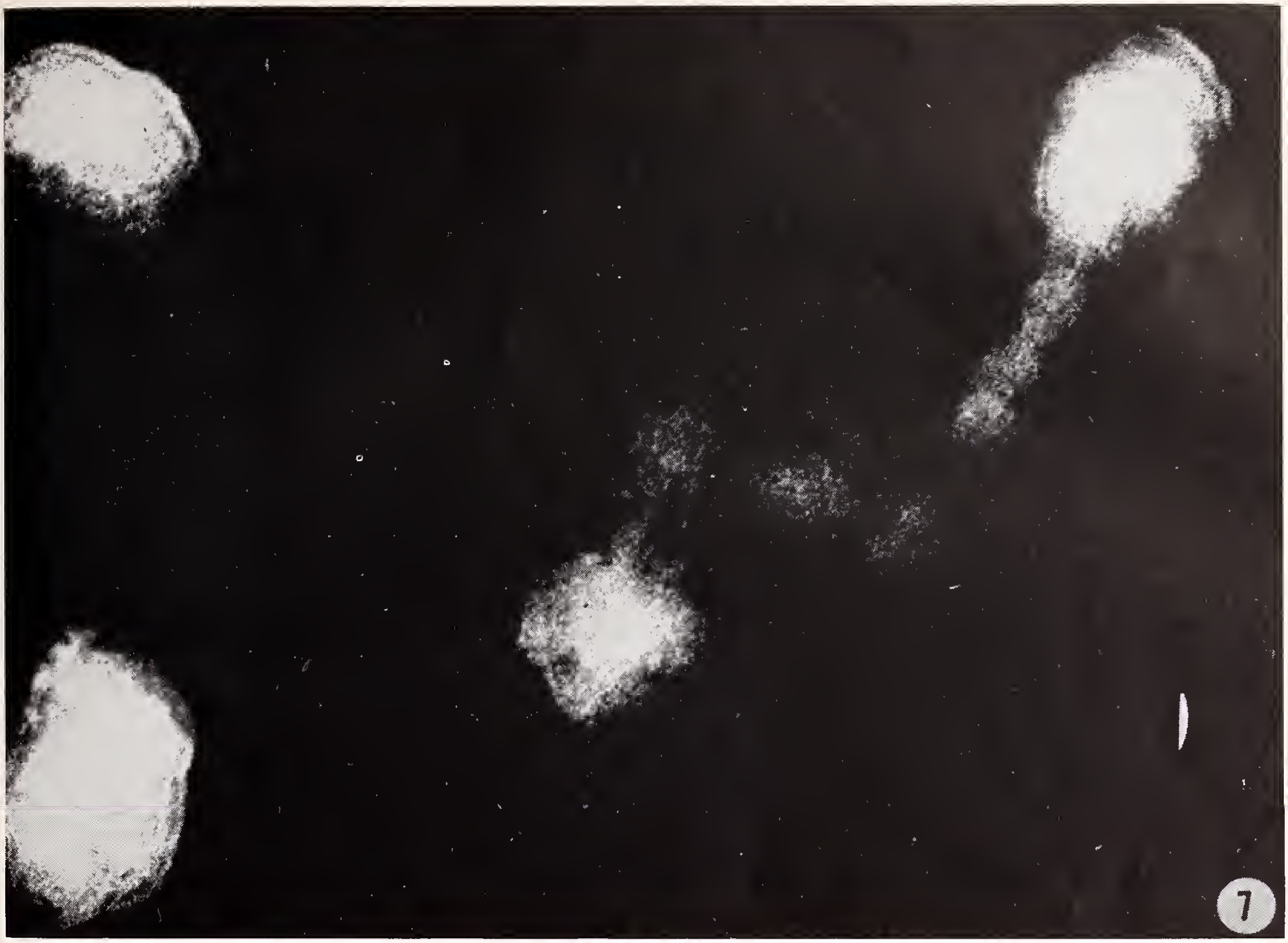


FIGURE VII

The same material as shown in Figure VI, illustrating internal and surface structure of the virus-like particles. Standard methods have so far failed to yield adequate pictures of surface structure. The intensity of staining with uranyl acetate suggests the presence of DNA. Magnification x 100,000.

the use of electron microscopy in the routine diagnosis of disease in certain selected cases. The most important of these would appear to be group identification of virus particles in material from skin lesions or tissue fluids from lesions suspected to be of viral etiology, and in the identification and quantitative evaluation of particles believed to be viral in nature present in the serum.

Acknowledgements

Dr. Joseph L. Melnick of the Department of Virology and Epidemiology, Baylor University College of Medicine kindly provided helpful information and permission to reproduce Figure III and IV. Miss Lillemor Wallmark provided expert technical assistance and Mrs. Madeleine Strauss assisted in final preparation of the manuscript.

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Laboratory Investigation Of Absent Or Diminished Menstruation

Nathan Kase, M.D. and Clarence D. Davis, M.D.

■ Intelligent utilization of the laboratory for the investigation of abnormal menstruation requires a thorough understanding of the various interdependent endocrine factors which regulate normal menstrual function. Though knowledge in this area is incomplete, current concepts of the neuro-endocrine-target organ relationships permits a reasonably precise laboratory dissection of the basic hormonal components and the functional levels of these elements in normal and abnormal states. Many reviews of the physiology of menstruation are available: that of Mazer and Israel[1] is particularly recommended. This paper assumes working knowledge of these fundamentals. In addition, it deals only with the *laboratory investigation* of absent or diminished menstruation.

It is not economically feasible to utilize every laboratory test for every patient under study. For this reason certain arbitrary categories defining abnormal activity must be constructed. The following definitions are currently utilized in our Gynecologic Endocrine Clinic to determine which situations require active study:

1. Primary amenorrhea past the age of 16; earlier, if associated with delayed pubarche or theelarche.
2. Secondary amenorrhea (in the absence of castration or pregnancy) of at least 3 months duration.
3. Oligoamenorrhea: Intervals of two or more months between menses, particularly when preceded by normal cycle intervals.
4. Hypomenorrhea: Marked and repetitive diminution in amount of flow measured in duration *and* napkin or tampon requirement.

All patients with these complaints deserve thorough evaluation. This includes endocrine studies to support the clinical impression and supplement other diagnostic studies. If hormonal medication has been recently administered, investigation is postponed until two months after withdrawal of therapy.

The following table is composed of pertinent laboratory tests currently available at either the Yale Gynecologic Endocrine Laboratory or the Medical Chemistry Laboratory.

A. *Pituitary:*

1. Urinary gonadotrophins ("FSH"). This requires a 24 hour urine collection. Values are expressed in mouse uterine units (m.u.u.). Normal adult range is 6.5-52.0 m.u.u./24 hours. In prepubertal children gonadotrophins are undetectable at the 6.5 m.u.u. level.
2. Metapirone suppression test. This involved test is used to determine pituitary and adrenal reserve.

B. *Ovaries:*

I. *Hormone Excretion.*

   a. Urinary pregnanediol. A 24 hour urine specimen is necessary. In excess of 2.5 mgm /24 hours indicates presence of corpus luteum function or pregnancy. Date of LMP should be included with request.

   b. Urinary total estrogens. This is done on a 24 hour urine specimen. Normal range is 10-75 micrograms/24 hours. The values will vary with the cycle. The date of the LMP should be given.

II. *Hormone Effects.*

   a. Cornification of vaginal smear. Above 3-5 per cent fully cornified cells indicates normal estrogen production. The cornification varies with the cycle. Date of LMP should be known.

   b. Endometrial biopsy.

   c. Presence or absence of arborization pattern of dried cervical mucus ("fern test").

   d. Basal body temperature curves.

C. *Adrenals:* All urine tests should be done on a 24 hour specimen. When ACTH stimulation is stipulated this refers to an intravenous dose of 40 units given over eight hours with simutaneous collection of a 24 hour sample of urine.

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1. 17 Ketosteroids (17 KS). Normal female range is 5-15 mgm/24 hours. Normally there is a 100 per cent increase after ACTH stimulation.
2. 17 Ketogenic steroids (17 KGS). Normal female range is 6-18 mgm/24 hours. 200 per cent normal rise following ACTH stimulation.
3. Pregnanetriol. Normal values are: prepubertal under 1 mgm/24 hours, post puberty under 3 mgm/24 hours.
4. 17 Ketosteroid fractionation for levels of dehydroepiandrosterone and 11-oxygenated 17 KS.
5. Plasma cortisol. This requires 10 ml. whole blood. Normal range is 12-24 micrograms per cent but following ACTH, 33-55 μg per cent.

D. *Thyroid:* PBI, BMR.

E. *Cytology:* Buccal or vaginal smear for determination of chromosomal sex. At least 10 per cent of the cells must be chromatin positive for a diagnosis of genetic female.

A single 24 hour urine specimen, collected in a clean vessel, refrigerated while collected, can be used for determination of FSH, pregnanediol and pregnanetriol, 17 KS and 17 KGS, and total estrogens. It is important to give careful instructions on collecting a 24 hour specimen. The patient must be cautioned to *discard* the 7 a.m. specimen before starting the 24 hours and to *include* the 7 a.m. specimen on concluding the collection.

The following table (modified after Israel) demonstrates the *various etiologic possibilities* confronting the physician in a patient with amenorrhea.

A. *Central Nervous System* (*Suprasellar*).
1. psychogenic
2. neurogenic
    - intracranial tumors, scars
    - vascular anomalies
    - internal hydrocephalus
    - hypothalamic disorders including those associated with obesity and lactation
    - Laurence-Moon-Biedl syndrome

B. *Pituitary:*
1. pituitary cachexia
2. tumors with or without lactation
    - chromophobe
    - eosinophile
    - basophile

C. *Ovaries:*
1. primary and secondary hypogonadism (including hypofunction)
2. ovarian agenesis (gonadal dysgenesis)
3. polycystic disease
4. tumors

D. *Uterine Disorders:*
1. congenital
2. acquired

E. *Thyroid Disease.*

F. *Adrenal Disease.*

Suprasellar And Pituitary

Altered menses may be the earliest sign of a suprasellar or pituitary lesion. Localization of such a disorder is usually obvious after consideration of the history, physical, and neurologic examination and specific roentgen studies. If these other data are inadequate, differentiation between central and target organ malfunction can often be made by urinary gonadotrophin determination. Low levels (under 6.5 m.u.u./24 hours) indicate an amenorrhea of central origin whereas high levels, (over 100 units) support a diagnosis of ovarian failure. Tumors of the CNS do not produce elevated gonadotrophins except in certain rare instances of precocious puberty. In these, a variety of tumors compressing the hypothalamus "set off" *precocious adult levels* of gonadotrophins. (Pregnancy, presenting an extrapituitary source of gonadotrophins, will give values of 208 m.u.u. and higher associated with amenorrhea).

Normal gonadotrophin production is usually associated with a characteristic fern pattern of the cervical mucus and with vaginal cornification, both of which can be tested easily in the office. However, the presence of normal levels of gonadotrophins as determined by these simple tests or by specific laboratory bioassay does not always exclude a CNS etiology for amenorrhea. Psychogenic amenorrhea may be associated with normal or low gonadotrophins. Pituitary tumors may be so small that they do not exert pressure suppression of gonadotrophins yet may lead to amenorrhea by peripheral effects on target organs. As such a tumor enlarges it will lead to absence of gonadotrophins as well as more obvious neurologic, ophthalmic, and roentgen signs.

Ovarian

The extreme case of irreversible ovarian failure (primary or secondary hypogonadism) is represented by high FSH (over 100 m.u.u.), low urinary estrogen (under 10 μg/24 hours and/or less than 3 per cent vaginal smear cornification) and very low noncyclic pregnanediol excretion. In ovarian agenesis, in addition to these features of ovarian failure, 80 per cent of the cases show a male chromatin pattern on buccal or vaginal smears.

However, the ovarian response to polypeptide hormone stimulation does not adhere to an "all or none" principle. In many instances the ovary may exhibit noncyclic or abnormal steroid hormone production despite apparently normal levels of gonadotrophin. Anovulatory oligo-amenorrhea, characterized by non-cyclic menses, normal to low urinary estrogen excretion, and rare corpus luteum function (monophasic basal body temperatures, persistent fern pattern, absent progestational effects on biopsy and vaginal smear, and low non-cyclic pregnanediol urinary excretion) is seen in the multiple varieties of pituitary-ovarian derangements attending such factors as extremes of diet and severe psychologic and psychiatric stress. Polycystic ovarian disease is perhaps the most marked example of arrested ovarian follicle maturation associated with rigid "dampening" of the pituitary-ovarian servomechanism. Accumulating evidence indicts excess ovarian production of testosterone as responsible for most of the clinical aspects of the syndrome. Unfortunately, specific measurement of this steroid in blood and urine is not routinely available. Furthermore, the unusual biologic activity of testosterone allows considerable endocrine function to exist without alteration in androgen metabolites in urine. For this reason, 17 KS excretion is usually within normal range in this syndrome despite presence of hirsutism, male escutcheon, and uterine atrophy. The normal 17 KS excretion allows differential diagnosis of this syndrome from abnormalities of the adrenal gland in which 17 KS, 17 KGS, pregnanetriol, 11-oxygenated 17 KS and other metabolites specifically produced by the adrenal cortex are elevated. At the moment the laboratory diagnosis of polycystic ovarian disease is made by exclusion of adrenal abnormality.

A similar problem obtains in the masculinizing tumors of the ovary associated with amenorrhea. Again, small amounts of highly active steroidal androgen, presumably testosterone, cause marked endocrine changes without appreciable elevation of 17 KS in many cases. Only the adrenal rest tumor produces significant amounts of 17 KS, 17 KGS, pregnanediol, pregnanetriol as well as other typically adrenal steroids. In arrhenoblastoma, hilus cell tumor, or the adrenal rest, atrophy of the contralateral ovary, when present leads to marked diminution in estrogen production and activity.

Uterine Factors

The various congenital and acquired factors which lead to amenorrhea are suggested when a normal laboratory workup is encountered. This is particularly true if repeated evidence of cyclic ovulatory ovarian function is observed unaccompanied by external signs of menstrual response. Furthermore, the amenorrhea in these instances will display similar refractoriness to repeated exogenous pharmacologic doses of estrogen and progesterone.

Thyroid

In hyperthyroidism the more severe the toxicity the less the menstrual flow, amenorrhea indicating a severe disorder. The diagnosis rests on history, physical examination, and such laboratory aids as PBI, BMR, radioactive iodine uptake, etc.

Though oligo-amenorrhea is sometimes seen in hypothyroidism, menometrorrhagia is the rule. In hypothyroidism secondary to hypopituitarism amenorrhea does obtain. In this latter situation diminished gonadotrophins, estrogen, and progesterone production is demonstrable by laboratory means. In primary thyroid conditions these hormone deficiencies are less common.

Adrenal

A. Hyperfunction:

There are four clinical varieties of adrenal hyperfunction. In Cushing's Syndrome there is excessive production of corticosteroids, (C_{21}), while in the adrenogenital syndrome there is an excess of androgenic steroids (C_{19}). In a third group there is overproduction of both types of steroids. Lastly, a syndrome of hyperaldosteronism is recognized. While the first three profoundly effect menses, the fourth has no known gonadal influence.

1. *Cushing's Syndrome* is suspected from the history and characteristic physical findings. Confirmatory laboratory evidence includes elevated blood cortisol, decreased glucose tolerance, diminished serum proteins, polycythemia, eosinopenia, and lymphopenia. Although amenorrhea occurs frequently (70-80 per cent) gonadotrophins are normal. Ovarian activity as determined by laboratory investigation may be preserved and pregnancy is possible.

2. *Adrenogenital syndrome.* This term applies to hyperplasia or tumor of the adrenal cortex unassociated with glucocorticoid excess or effect and characterized by high 17 KS production, amenorrhea, and virilization. The laboratory differentiation of this syndrome from ovarian abnormalities rests on the degree of elevation of 17 KS, the presence of elevated 11-oxygenated 17 KS on fractionation of total 17 KS, and increased pregnanetriol excretion. Generally speaking hyperplastic adrenals can be stimulated to increased hormone production by exogenous ACTH or suppressed by administration of cortisol (or one of its derivatives), whereas tumors do not respond

to such stimuli. However, exceptions have been encountered in both tumor and hyperplasia so that the differential diagnosis must rest on a complete analysis of all the data.

3. Combined glucocorticoid and androgen excess is typical of adrenal lesions and adrenal rest tumors of the ovary. These display mixed laboratory evidence of abnormal adrenal steroid production (17 KS as well as cortisol and metabolites).

B. Hypofunction (Addison's Disease).

This disease is rarely associated with menstrual abnormality or anovulation. In profoundly affected individuals amenorrhea may ensue on the basis of inanition. The laboratory diagnosis is based on the flat glucose tolerance curve, low serum sodium and high potassium, and the low 17 KS, 17 KGS, and cortisol none of which rise normally after ACTH administration.

The cases seen in the Yale Gynecologic Endocrine Clinic represent a highly selected sampling of oligo-amenorrhea. Prior to referral, almost all extragonadal causes of diminished menses have been withdrawn from the patient pool. Therefore, the primary interest in the clinic has been in the less specific area of pituitary-ovarian derangements. A subsidiary classification of these disorders has been found helpful particularly from the point of therapy. It is based on a laboratory estimation of the relationship of gonadotrophin and estrogen activities:

A. Hypergonadotrophic oligo-amenorrhea

B. Normogonadotrophic oligo-amenorrhea
  1. hypoestrogenic
  2. normoestrogenic

C. Hypogonadotrophic oligo-amenorrhea

Excluding normal menopause, hypergonadotrophic hypogonadism is seen in approximately 10 per cent of our cases. This group includes gonadal dysgenesis of various types as well as premature irreversible hypogonadism of undisclosed etiology. Replacement therapy for target organ support is currently the only therapy available.

Normogonadotrophic oligo-amenorrhea occurs in about 60 per cent of our cases. Of these, the hypoestrogenic form is more frequently seen. This general group is composed of menstrual disorders associated with psychologic and psychiatric stress, obesity, or precipitous dieting. Various dysfunctional ovarian states, including the polycystic ovary syndrome, are also found in this group. In the simplest situation reversal of amenorrhea occurs either spontaneously or upon withdrawal from stress. Improved dietary habits are very often associated with return of normal menses. Periodic estrogen and progesterone therapy may be required to induce menstruation before normal menses recur. In specific situations the administration of cortisone (and derivatives) or operative intervention by wedge resection may be required. An experimental drug, Clomiphene citrate gives promise of extraordinary usefulness in this general group of normogonadotrophic amenorrhea.

Some 30 per cent of our cases are hypogonadotrophic hypogonadal individuals. This unusual preponderance results from diagnostic as well as therapeutic interest in hypogonadism secondary to disordered hypothalamic-pituitary relations. In these cases experimental administration of relatively pure human pituitary FSH and human chorionic gonadotrophin (HCG) as well as therapy utilizing purified human menopausal urinary FSH plus HCG has been undertaken by members of our department. Ovulation can be induced in this way, pregnancies having resulted under both regimens. Short of general availability of such gonadotrophins, target organ support by cyclic estrogen replacement therapy is advised in these cases.

The foregoing paragraphs demonstrate that laboratory facilities can adequately supplement other findings to achieve accurate diagnosis and appropriate therapy in cases of altered menses.

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Opportunistic Fungus Infections

Leanor D. Haley, Ph.D.

■ Some fungi causing disease in man do so only when the host's defenses have been altered through disease or certain forms of chemotherapy. These fungi are most often referred to as "opportunists." They include species of Aspergillus, Candida, Cephalosporium, Fusarium, Rhizopus and Mucor as well as other genera. Other fungi capable of producing primary infection in man may also be considered "opportunistic" under certain conditions such as disseminated cryptococcosis in Hodgkin's disease, nocardiosis in patients with pulmonary alveolar proteinosis, and histoplasmosis in patients with lymphomas. The increasing incidence of these systemic fungus infections throughout the country makes this a timely subject for review.

The factors that enable an opportunistic fungus to cause an infection are not clearly understood, or even known in some instances. There is no doubt that the diabetic patient is very susceptible to Rhizopus infections of the nasal sinuses and the central nervous system, but this is only true of the poorly regulated diabetic who has frequent episodes of acidosis. Bauer and associates[2] demonstrated experimentally that hyperglycemia alone does not enable Rhizopus to set up an infection such as is seen in rabbits with acute alloxan diabetes and renal acidosis. Sheldon and Bauer[6] demonstrated in rats experimentally infected with Rhizopus and which had acute alloxan diabetes a delay in the release of granules from the tissue mast cells in association with a delayed inflammatory response during which time the fungus rapidly spread throughout the tissues. Other factors, however, must be involved, for in the normal rat whose mast cells had been degranulated with drugs, delayed development of an inflammatory reaction occurred as in the alloxan diabetic rats, but an active fungus infection with Rhizopus did not develop.

Administration of corticosteroids may enable an opportunistic fungus to set up an infection or cause dissemination of a fungus from a localized lesion. Mycotic ulcerative keratitis is an excellent example of an opportunistic fungus infection developing after the topical use of steroids. This fungus infection is secondary to a superficial corneal lesion resulting from a bacterial or viral infection, chronic glaucoma with corneal edema, or from the introduction of a foreign body such as a cigarette ash. Zimmerman[10] has reported that histopathologic study of enucleated whole eyes examined between 1952-1956, before corticosteroids were used in great quantities, revealed that one eye per 413 eyes had keratomycosis; those eyes examined between 1957-1961 showed one eye per 229 eyes with this infection. These figures did not include corneal buttons obtained at time of keratoplasty or sections of eyes received from other laboratories.

Why corticosteroids enhance fungus infections is not known. Perhaps the suppression of cellular and humoral defense mechanisms of the host by these drugs is the significant explanation, but not the complete one.[4] It has been suggested that fungi can actually utilize some of these compounds as growth factors.[5]

The use of antibiotics also has prepared the way for opportunistic fungus infections, but, again, little understanding of the mechanisms involved exists. The most common explanation is that the antibiotics upset the normal microbial ecology of the host, permitting certain fungi to cause disease. *Escherichia coli* and certain other species of enterobacteria will suppress the growth of Candida *in vitro* and in the urinary tract; removal of these bacteria with antibiotics may enable a fungus to establish itself in numbers great enough to overcome, at least locally, the host's defense mechanism.

Some opportunistic fungi grow in old lesions as saprophytes. A good example of this is seen in the aspergilloma or fungus ball. It must be recognized, however, that such localized colonies of a fungus may be a potential source of a disseminated mycotic disease should the host defenses deteriorate through a debilitating disease or use of certain chemotherapeutic agents.

It is obvious that our knowledge of the immunologic and physiologic factors that play a significant role in any fungus infection is scanty.

Occasionally an opportunistic fungus infection may be the indicator of an unsuspected underlying disease. Sutphin,[7] Whitaker and associates[9] have observed candidiasis of the skin, nails, and mucous membranes in a significant number of patients who were later found to have hypoparathyroidism.

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These infections were established before chemical analysis revealed a fall in calcium level. They suggested that atrophy of the skin due to the hormonal disturbance permitted the Candida to set up an infection.

Wehner and associates[8] reviewed a number of their cases of pulmonary aspergillosis and found that three of their four cases of the invasive form of this disease were in children of the age of four or younger. They proposed that these patients had a deficiency in their immune mechanism; unfortunately, these cases terminated in death and further studies were not made.

Candida granuloma is a serious form of candidiasis seen in children which also appears to be related to a deficiency in the immunologic response of the patient. These patients often die following innumerable reoccurring bacterial and mycotic infections.

Callaway[3] reported a case of widespread *Trichophyton rubrum* infection in a five year old girl which had persisted for three years. The infection failed to respond to all treatment despite the fact that *in vitro* studies revealed the fungus to be sensitive to griseofulvin and several other anti-mycotic agents. The child suddenly developed a low grade fever and enlarged liver and spleen; following intensive medical studies, the diagnosis of aleukemic lymphatic leukemia was established.

It is apparent then that repeated isolation of any fungus from a serious infection, particularly if it be one of the "opportunistic" fungi, should inspire the attending physician to search deeply for an underlying disorder.

The assistance which the laboratory can offer to the physician whose patient is suspected of having an infection caused by one of the opportunistic fungi is limited but still significant. Cultures are of little value unless accompanying direct microscopic studies of the clinical specimens are also made. Spores and even fragments of hyphae of Aspergillus, Penicillium, Fusarium, and other saprophytic fungi are in the air and easily find their way to the upper respiratory tract and the gastrointestinal tract, as well as to the skin surface. These fungi are frequently seen on plates in both the mycology and bacteriology laboratories as contaminants. It is necessary to demonstrate the fungus microscopically in repeated clinical specimens and to isolate the same species each time. Even the microscopic demonstration of the fungus in clinical material must be interpreted with care.

The most common form of pulmonary aspergillosis is a localized growth of the organism on the surface of old cavities, in cysts, or even along the walls of bronchi. There is no invasion of tissue and little pathology may develop as a result of this growth. Hence, a microscopic preparation revealing Aspergillus in the specimen does not necessarily indicate anything more than that the fungus is present, perhaps as a saprophyte. On the other hand, failure to demonstrate Aspergillus in sputum or bronchial aspirates does not rule out aspergillosis. The more serious form of aspergillosis is the invasive type in which the fungus invades tissues, causing abscesses or a chronic progressive granulomatous disease. It may even invade blood vessels resulting in dissemination of the fungus throughout the body. Only by obtaining tissue can the fungus be demonstrated. Laboratory studies will usually fail to reveal the fungus in sputum specimens of patients with an aspergilloma.

With Candida also it is necessary to demonstrate the hyphae repeatedly in clinical specimens before any significance can be assigned to positive cultures. Candida species are also found in the upper respiratory tract, the gastrointestinal tract and on the skin as part of the normal microbial flora.

If the laboratory can demonstrate the typical broad, non-septate, brown hyphae of Mucor or Rhizopus in a specimen, this may be indicative of the presence of phycomycosis (mucormycosis). Although cultures may yield these fungi, the hyphae are not found in the clinical material in the absence of an infection. It must be pointed out, however, that a properly collected specimen is essential. Washings of the nasal sinuses are unlikely to reveal the fungus since it is invading tissue. Curettings of the turbinates or of necrotic tissue must be obtained.

A proper specimen is also requisite when the physician is attempting to establish the diagnosis of mycotic ulcerative keratitis. The mycotic agent grows deep in the ulcer as well as in the adjacent corneal stroma. The insertion of swabs into the lesion will not yield material in which the fungus is present. It is necessary to scrape the lesion with a Bard-Parker blade or some similar instrument. The physician should make two smears of the tissue fragments (do not heat fix) and then place the blade into a tube of Sabouraud's broth. These are sent to the laboratory for fungus stains and cultures. Zimmerman,[10] Anderson[1] and others have stated four basic steps that must be taken quickly if the physician hopes to treat sucessfully mycotic ulcerative keratitis: 1) early diagnosis, 2) withdrawal of corticosteroids, 3) removal of necrotic tissue, and 4) application of fungicides. Indeed, no opportunistic fungus infection requires a diagnosis any more quickly than does that of mycotic ulcerative keratitis or phycomycosis.

Summary

The brief discussion presented in this paper on the nature of opportunistic fungus diseases points out at least two facts. First, the medical student's rhyme "There is fungus among us" is not a joke, for it is the fungi often making up a portion of the normal microbial flora of man that are most frequently the etiologic agents for these diseases. Secondly, any attempt to explain the mechanisms of the pathogenesis of these diseases on one or two factors is unrealistic. Liebig stated ". . . we are too much accustomed to attribute to single cause that which is the product of several. . . ." It is obvious from the work presented in this paper as well as in others that many factors may be involved; our knowledge of these factors is scanty.

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> The scientist who achieves intellectual and emotional maturity without losing his investigative vitality and courage—that is without metaphysical surrender—can come to rest in philosophical tranquillity with the recognition that science, however highly developed may never answer the ultimate questions, but that there may be happiness in contemplating nature's orderly coordination and peace in modest fellowship with the rational and humane spirits who, throughout the brutalities of history, have held to the purpose of reason. Complete comprehension could add very little.
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> —H. Zinssen, *Rats, Lice and History.*

The Connecticut Registry–Its Importance And Contributions To Oncology

Henry Eisenberg, M.D.

■ Thirty years have passed since the House of Delegates of the Connecticut State Medical Society initiated a resolution requesting its Council to ask for the formation of a Tumor Study Committee.* The Council approved the resolution and two years later the committee suggested that the Connecticut State Medical Society sponsor a bill in the legislature which subsequently was passed by the General Assembly in 1935. The important part of the bill reads as follows: "The State Department of Health is authorized to make investigation concerning cancer, the prevention and treatment thereof and the mortality therefrom, and to take such action as it may deem will assist in bringing about a reduction in the mortality due thereto."

This bill resulted in the establishment of the Division of Cancer Research and subsequently within this division, The Central Cancer Registry in 1941, whose first director was Dr. M. H. Griswold. During the first five-year period from 1936-40, the activities of the division were confined to providing mortality statistics, public and professional education and aiding in the establishing of tumor clinics. The Tumor Study Committee of the State Medical Society, which later changed its name to the Cancer Coordinating Committee, continued to give guidance to the overall cancer program in the State. Among some of the chairmen were Drs. C. L. Larkin, E. Liebow, A. Ryan and presently W. Mendelsohn. The extensive coverage of the field of cancer control in Connecticut is made possible by the close coordination of the activities of this committee with the Connecticut Chapter, American Cancer Society headed by its Executive Director, E. Meiss, and with the State Department of Health.

In 1941, a team consisting of a physician, a statistician and specially trained clerks, visited each hospital to prepare abstracts of all cases of cancer admitted to these hospitals after the first of January 1935, leaving the original at the source, which established the local registry and incorporating a copy in the Central Registry.

Now, all hospitals in the State of Connecticut (non-profit, private and state) provide the Central Registry with prepared abstract forms of all new cases of cancer diagnosed and later with life-long follow-up surviving cancer patients. The Public Health Statistics Section of the State Health Department supplies the Cancer Registry with a copy of all the death certificates on which mention of cancer has been made.

The Cancer Registry is now called the Connecticut Tumor Registry and has on file approximately 165,000 tumors, both malignant and benign, of which approximately 60,000 are under active follow-up. Over 8,500 new cases and another 1,000 new second primaries are currently added to this roster yearly. The Connecticut Registry is the only registry within the United States which is based upon a defined population group, namely the State of Connecticut. Such a population-based registry permits statistical analyses which provide incidence rates, survival, and mortality rates by sex, age, stage, site and treatment.

Other cancer registries have been established in the United States since 1935, but none is as inclusive in its scope and collection of data as is the Connecticut Tumor Registry. Because of this, the Connecticut Registry provides information concerning the size and the nature of the cancer problem in this state, and often its data are projected to the scope of the national problem. It has provided information for the evaluation of the progress of this disease and the effectiveness of the treatment provided for it. The data from the Registry lead to information on trends in cancer incidence, accuracy of diagnosis, stage of disease at diagnosis and the development of theories concerning the etiology of cancer. Testing of such theories could bring about knowledge to be translated into cancer control measures.

These contributions have brought about the recognition of the importance of the Connecticut Tumor Registry. Due to the wide distribution of its publications it has become known to numerous researchers in the field within the United States and in many foreign countries. The publication of a

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monograph, "Cancer in Connecticut, 1935-1951"* published in 1955, has contributed immeasurably to analyses and comparison of data gathered in various parts of the nation and in foreign countries.

Cooperation With The National Cancer Institute

Due to its long history and its unique property of being based on the total population of a state, the Connecticut Tumor Registry is the most important contributor to the End Results Evaluation Section of the National Cancer Institute of which it is a member.

The End Results Evaluation Program itself is an outgrowth of the Symposium on End Results in the Treatment of Cancer at the Third National Cancer Conference, June 1956. At the symposium, end-results information on 66,000 patients from three central registries, 11 individual hospitals, and 21 individual cancer specialists was presented. However, the data were limited in scope, and the comparability of data collected at the various institutions was questionable because of differences in definition of terms, selection of patients, and follow-up policies.

The Symposium on End Results led to a recognition of the desirability for a continuing program of cooperation and coordination among the various registries in order to provide comparable data and to make possible the pooling of resources for research activities. The recognition of the need for a coordinated registry program coincided with a sizable expansion of cancer chemotherapy research activities. This accentuated the desirability for long-term follow-up information to relate the results of chemotherapy to those achieved by other means of treatment. The Cancer Chemotherapy National Service Center, the administrative unit for the chemotherapy research program, invited the registries that had submitted usable information to the Third National Cancer Conference to join in a cooperative program for the evaluation of end results in cancer. At an organizational meeting in September 1956, the National Cancer Institute offered to support the research effort through contracts providing for the submission of specified data on an annual basis, and by providing a technical and administrative staff to coordinate the activities of the individual participants. The proposed program was accepted by the registries and was endorsed by representatives of the American Cancer Society, the American College of Radiology, the American College of Surgeons, the Association of Tumor Clinic Registrars, and the College of American Pathologists.

A series of work shops followed, leading to agreement on a uniform punch card layout and code for the submission of diagnostic, treatment, and follow-up information on individual patients. Based on this, studies of less frequently occurring tumors can be done by pooling the data of the cooperating registries. Such studies are presently underway.

Data Processing

More and more cancer data are becoming available every day and are being processed more rapidly than ever before. From the beginning, the Tumor Registry has utilized IBM equipment to handle its data collection and has kept up with the development of faster and newer IBM machines. Presently, most of the evaluative analyses is being done by advanced computer techniques, permitting answers to urgent questions in as short a time as possible. The Registry is constantly contacted by individual physicians requesting information on the evaluation of specific treatment methods in reference to survival of patients with specific types of cancer.

Prior to 1957, processing of Connecticut cancer research information involved transferring by hand the information reported by hospitals to the Central Registry and posting the follow-up information on simple filing cards. Follow-ups of recorded cases, again, were merely filed with case records later to undergo statistical analysis.

However, in 1956, after its affiliation with the National Cancer Institute, the Registry acquired a large number of IBM Data Processing machines and was able to establish a punch card follow-up system.

Quality Control

In 1960, the Connecticut Tumor Registry established a new and comprehensive analytic cancer code which became operational in 1961. This code is compatible with the Uniform Punch Card code used by the NCI End Results Evaluation Section, which in turn, is in line with the code of the World Health Organization. To insure uniformity and good quality of the coding used to develop cancer statistics, a special computer program was developed to error check all analytic punch cards.

The Tumor Registry is now in a position to do extensive survival computations. This was proven when, with the help of the State's IBM 1401, the Registry was able to calculate survival rates of female patients with breast cancer according to different types of treatments.

International Studies

In the past, it has been difficult to compare the statistics collected in the Connecticut Tumor Registry with any other within the United States, since the Connecticut Registry is the only one which is based on a total population group. A great deal more information about the size and nature of the cancer problem and more extensive evaluation of the progress in the cancer fight could be made if such data from Connecticut could be compared with data from other central registries similarly based on total population groups. This is one more reason why, within the last few years, studies based on geographic epidemiology have become so important.

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In geographic epidemiology, the data from one part of a country are compared with data from an entirely different part of the country, or, better yet, with data derived from other countries. Similarly, the study of geographic pathology combined with geographic epidemiology could possibly bring forth information which eventually will lead to important clues in the general study of the Cancer Problem.

It is for these reasons that a cooperative study has been initiated between Norway, Denmark, and Connecticut which will analyze survival by separate parts of the colon (ascending, transverse, descending, and rectosigmoid) and will also try to clarify the criteria used in the various countries as to what is considered urban and rural areas.

In order to understand better the differences which exist between the data of leukemia coming from Denmark and Connecticut, another cooperative study will be initiated which will study the pathology of this disease. The study, considered to be one of geographic pathology, in addition to geographic epidemiology, will be done in cooperation with two hematologists—one from the United States and one from Denmark who will be requested to review blood slides from leukemia patients from Denmark and Connecticut. This undoubtedly will result in mutual agreement on definition and criteria of leukemia and will then permit cases of leukemia from Connecticut and Denmark to be compared with each other, in regard to age, sex, incidence and survival rates.

The central registries of Denmark, Norway and Finland, like the Connecticut Registry, organized and quite similarly operated, have been requested to describe in detail their criteria for diagnosis, stage, treatment and urban and rural areas. Only after such criteria have been mutually agreed upon by all concerned, can data be used for comparative observations between the statistics of these registries.

Future studies, especially with Finland, will be concerned with stomach, esophagus and breast cancers. It has been observed that incidence rates for stomach cancer have been gradually decreasing within Connecticut, as throughout the United States. This is not the case in Finland, where the incidence rates for stomach cancer are extremely high and the mortality rates are the second highest in the world, surpassed only by Japan.

The incidence rates of cancer of the esophagus in Connecticut are much higher in males than in females. However, this ratio is reversed in Finland. In Finland, also, the observation was made that among breast cancer patients the survival rate in the second five-year period for patients treated with radiation is much lower than for patients who did not receive any radiation but did receive surgical therapy.

These are only a few observations which need further investigation. It is anticipated that more cooperative studies between foreign countries and Connecticut will be instituted in the near future.

Contributions To Oncology

To date, fifty individual contributions have been made to the literature by members of the Registry staff alone or in cooperation with investigators from Connecticut and other states. Collaborators from Connecticut have included Drs. A. W. Oughterson, E. Ottenheimer, L. Ryan, T. L. Curran and M. H. Griswold. Some of the publications have covered the overall approach to the interpretation and analyses of the collective data. An important series of survival analyses incorporating two time periods, 1935-44 and 1945-54, done cooperatively by the Registry and the National Cancer Institute has dealt with such major sites as breast, uterus, ovary, stomach, and large intestine and rectum.

In breast cancer only slight improvement was seen in the relative five-year survival rate in the second time period when compared with the first, which was shown to be 50 per cent, while the rate in the 1945-54 period was 56 per cent. There was, however, no improvement in the ten-year survival rate.

The survival of patients with uterine cancer, that is, cervix and corpus, diagnosed during the second time period has displayed a markedly higher five-year relative survival rate than that for patients diagnosed during the earlier time period. Among treatment methods, surgery was strikingly successful in treating women with cancer of the cervix under age 55 with spread of the disease localized: nine out of ten of these patients survived five years.

The survival of patients with ovarian cancer in these time periods did not show any great change. However, the relative survival rate from the end of the fifth to the end of the tenth year improved from 79 to 93 per cent. The outlook for younger women, relative to general population mortality, was better than for older women.

Among patients with cancer of the stomach diagnosed 1935-44, about one out of five who were expected to survive the first year after diagnosis, in fact survived; of those expected to live from the end of the first year through the fifth year, one out of three survived. Mortality among the five-year survivors was far greater than that of persons in the general population of similar age. Patients diagnosed 1945-54 experienced slightly higher five-year survival than those diagnosed 1935-44; this improvement in length of survival was associated with an increase in the per cent of patients treated by surgical intervention and an increase in the survival time of the surgically treated patients.

The data on cancer of the large intestine and rectum, Connecticut 1935-54, are unique in that they describe the experience of virtually all patients with these diseases in a community rather than that of patients admitted to an individual treatment center. Observed survival is measured relative to expected survival in the general population. For cancer of the large intestine and rectum, five-year survivors experienced considerably higher mortality than persons of similar age in the general population. Ten-year survivors experienced approximately normal survival between the 10th and 15th years after diagnosis. Five-year relative survival rates improved dramatically from 1935-44 to the post-World War II period 1945-54; large intestine: males, 19 to 32 per cent; females, 23 to 39; rectum: males, 15 to 30; females, 23 to 32. Improvement was noted for patients with localized disease and with regional spread. The relative number of untreated patients decreased from 1 in 4 to 1 in 6 for cancer of the large intestine, and from 1 in 5 to 1 in 7 for cancer of the rectum. More frequent use of surgery and increase in length of survival of the surgically treated patients contributed to the over all improvement. Most of the increase in the five-year relative survival rate for the surgically treated patients resulted from increase in the one-year survival rate, which suggests that reduction of operative mortality was an important factor. Women tended to have a more favorable outlook than men, but for cancer of the rectum, this sex difference disappeared during the second period of diagnosis, 1945-54.

A depth study of 8,396 proven cases of breast cancer diagnosed between 1935-1953, was conducted by a team headed by Dr. Allan J. Ryan. This study demonstrated a significant increase in the five-year survival of cases treated with radical surgery plus radiation over other individual or combination of treatment. This advantage for radical surgery plus radiation does not seem to continue beyond five years according to unpublished data.

Several studies of mortality and incidence rates for various sites have shown that mortality data does not present a true picture of the incidence rate. The mortality rate underestimates the incidence rate by up to 20 per cent.

A detailed study of the relationship between the ABO blood groups and gastric cancer confirmed the association between A and gastric cancer reported by previous investigators.

A local surgeon has recently completed a depth study of 157 cases of anal cancer diagnosed from 1935-1959. This is the largest series ever investigated by a single investigator or team of investigators and was made possible by the records available in the Connecticut Tumor Registry.

A local head and neck surgeon is about to undertake a depth study of head and neck solid tumors with regard to the relationship of treatment and survival. All cases of prostate cancer are being reviewed by a local urologist to determine if changes in treatment initiated in the mid 1940's are reflected in a change in survival rates. Others have studied in depth, specific sites, geographic variations, diagnostic techniques and end results of the various treatment employed.

The Connecticut Tumor Registry contains information on over 160,000 cases of cancer and special interest "benign" tumors diagnosed from 1935 to the present day. Large numbers of rare types can be made available to pathologists and surgeons who wished to investigate virtually unexplored areas of oncology. For the more frequently occurring sites of cancer, a wealth of data exists which has not as yet been investigated but which might very well contain further clues to the Cancer Problem. The data collected by the Registry are primarily a result of the foresight of the State's physicians and are at their disposal to be utilized for "the prevention and treatment of cancer and to reduce the mortality therefrom." The final goal is to "take such action as . . . will assist in bringing about a reduction in the mortality due thereto." We cordially invite physicians having an interest in any field of cancer research which can be studied through our statistics to communicate with us with the object of setting up useful projects.

Breast Carcinoma: Histologic Grading And Survival In A Large Series Of Cases

Roy N. Barnett, M.D., and Henry Eisenberg, M.D.

■ The object of this study was to decide whether histologic grading of breast carcinoma was a useful prognostic tool. The necessity of obtaining such tools is self-evident if different modalities of treatment are to be compared; we must be confident that our comparisons deal with groups of patients as similar as possible.

A comprehensive discussion of problems of grading is given by Haagensen.[1] He originally established a system of grading[2] in which certain special cancers were studied individually; the common forms, comprising 71 per cent of no special type, were then graded as I, II or III in ascending order of malignancy. Results in 154 cases were:

Grade	*No. of cases*	*% of series*	*% of 5 yr. survivals*
I	40	26	80
II	66	43	38
III	48	31	13
All	154		41

Dr. A. P. Stout,[1] also at the Presbyterian Hospital in New York, collected a much larger series classified in similar fashion as follows:

Grade	*No. of cases*	*% of series*	*% of 5 yr. survivals*
I	*84*	7.6%	*78.6*
Limited to breast	52		86.5
Axillary metastases	32		65.6
II	*422*	38.3	*48.1*
Limited to breast	165		69.1
Axillary metastases	257		34.6
III	*597*	54.1	*32.8*
Limited to breast	202		59.9
Axillary metastases	395		19.0
All	1103	100.0	*42.2*

The problem of maintaining uniform criteria for each grade is suggested by these two series; even at the same institution, with an attempt at continuity, there was a marked shift towards the diagnosis of less cases of Grade I and more of Grade III over the years. This apparently resulted in shifting patients with less ominous disease into higher grades and improved the prognosis in the higher grades.

In his authoritative Tumor Fascicle[3] Stewart is sufficiently disillusioned with grading to state "Appropriate anatomic histologic classification obviates the need for grading." Haagensen[1] tested this hypothesis by studying only carcinomas of no special type. He concluded "Microscopic grading gives us useful information regarding the prognosis of this large group of carcinomas of no special type. I therefore believe that microscopical grading, used within the limitations that I have suggested, has a practical value and should be continued and encouraged."

There have been a few more recent studies of this subject. Bloom *et al*,[4] using a classification similar to Haagensen's, studied a considerable series including 86 completely untreated patients. He found a good correlation between grade and prognosis in both the treated and untreated groups. Hultborn and Tornberg[5] used a set of histologic criteria somewhat different from those of Haagensen to study a group of 517 cases treated at the Radiumhemmet from 1930 to 1955. They also employ 3 grades. Their results, using "corrected" survival rates were:

Grade	*% of series*	*% of 5 year survivals*
I	10	98
II	50	78
III	40	37
		——
		63

It was our hope that a retrospective study based on the comprehensive statistics of the Connecticut Cancer Record Registry might indicate the practicability and usefulness of grading on a large scale.

Material And Methods

In 1932 the Connecticut Association of Pathologists established uniform criteria for the histologic grading of breast carcinoma. The categories were:

Grade I—mature, well-differentiated.

Grade II—moderately immature, partly differentiated.

Grade III—immature, undifferentiated.

Grade IV—not stated.

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It was recognized that formal written criteria could be interpreted in different ways. The group of pathologists at first met frequently for case discussion till reasonable uniformity of grading in individual cases could be achieved. Since that time, as new pathologists have joined the hospital staffs, their senior confreres have indoctrinated them into the established criteria for grading. The criteria for Grades I, II and III were those of Haagensen;[3] Group IV is the group in which for some reason histologic grading was omitted.

In 1961 a questionnaire was sent to all the hospitals in the state to ascertain which had used the classification from 1935 to 1956, the period we wished to study. We found that there were nine such hospitals; all were good-sized and there was satisfactory continuity in pathologists to assure a reasonable adherence to the criteria from year to year. The hospitals were Bridgeport Hospital, Bridgeport; Charlotte Hungerford Hospital, Torrington; Hartford Hospital, Hartford; Middlesex Hospital, Middletown; New Britain General Hospital, New Britain; St. Francis Hospital, Hartford; St. Mary's Hospital, Waterbury; Hospital of St. Raphael, New Haven; and Waterbury Hospital, Waterbury.

A total of 5770 cases of breast cancer had been diagnosed with histologic verification in these institutions from 1935 through 1956. These cases were analyzed using computers and the following aspects studied:

1. Relative and cumulative survival rates.
2. At 5 and 10 years after diagnosis.
3. For each of the following age groups
   a. Under 35
   b. 35-44
   c. 45-54
   d. 55-64
   e. over 65
4. For patients without demonstrable metastases and with regional metastases.
5. For histologic grades I, II, III and IV.
6. Number of patients surviving at 10 years in each grade with regional and localized original disease.

The methods of calculating survival rates have been described previously.[6] In brief the relative cumulative survival is the percentage of actual survivors divided by the percentage of survivors which would be expected in a group of women of the age distribution under study. In certain categories the number of cases was too small for meaningful analysis; we identified these categories because their Standard Error (SE) exceeded 10, and they are in parentheses in our Tables.

Results

The results are presented in six Tables.

Table I indicates the total number of cases in each grade. It is apparent that Grade I, the best differentiated, is the least common, and that Grade II is the usual variety.

Table II gives the relative cumulative survival for each grade at 5 and 10 years. There is a very obvious correlation between grade and survival in each series at both 5 and 10 years, Grade I showing the greatest and Grade III the least percentage of survival. The survival in Grade IV, the unclassified group, is very close to the overall average.

From Table III we have some indication that the most differentiated tumors occur to a greater proportion in the older age groups. However even if old age influenced survival favorably this alone could not account for more than a small proportion of the better survival of Grade I patients observed in Table II.

Table IV demonstrates that for the whole series of staged cases slightly over half had regional spread at the time of diagnosis. Furthermore there is a clearcut correlation between histologic grading and the presence of regional spread; the less differentiated the tumor the more apt it is to have spread beyond the breast at the time of the original surgery. Table V gives the breakdown of survival for

Table I

ALL CASES BY GRADES 1935-1956		% OF ALL CASES	% OF THOSE GRADED
Grade I	426	7	10
II	2549	44	58
III	1415	25	32
IV	1380	24	
All Cases	5770	100	100

Table II

RELATIVE SURVIVAL, 1935-1956
CASES AT

	5 YRS.	10 YRS.
Grade I	92	86
II	64	51
III	49	39
IV	57	48
All Cases	61	50

Table III

AGE DISTRIBUTION FOR EACH GRADE, 1935-1956

	UNDER 45		45-54		55-64		OVER 64	
	NO.	%	NO.	%	NO.	%	NO.	%
Grade I	95	23	91	21	87	20	153	36
Grade II	517	21	645	25	665	26	722	28
Grade III	357	25	365	26	323	23	370	26
Grade IV	283	21	350	25	353	26	394	28
All Cases	1252	22	1451	25	1428	25	1639	28

each grade as influenced by the stage; again the importance of grading is seen, as well as the adverse effect when spread was already present.

Table IV
Incidence of Regional Spread
By Grades, 1935-1956: Expressed As Percentage

	LOCAL	REGIONAL SPREAD
Grade I	85	15
II	46	54
III	35	65
IV	46	54
All Grades	46	54

Table V
Relative Cumulative Survival At 5 and 10 Years By Stage and Histologic Grade; Cases Diagnosed 1935-1956

	5 YEARS		10 YEARS	
	LOCAL	REGIONAL	LOCAL	REGIONAL
Grade I	95	80	91	64
II	85	52	74	36
III	72	40	62	31
IV	80	47	71	36
All Cases	83	48	73	35

SE under 10 per cent in all categories

Table VI
Number of Cases Surviving at 5 and 10 Years By Stage and Histologic Grade; Cases Diagnosed 1935-1956

	5 YEARS		10 YEARS	
	LOCAL	REGIONAL	LOCAL	REGIONAL
Grade I	256	37	143	23
II	689	530	324	211
III	245	259	106	110
IV	289	200	122	81
All Cases	1479	1026	695	425

Table VI gives the number of patients from whom the 5 and 10 year relative cumulative survival rates were calculated. The numbers are obviously of considerable size.

Summary And Conclusions

In a series of 5770 patients with carcinoma of the breast treated in 9 Connecticut hospitals between 1935 and 1956, histologic grading was performed by the technique of Haagensen. There was found to be substantial prognostic value to such grading when 5 and 10 year cumulative survival rates were calculated; this was true for patients with and without regional lymph node metastases. Grading appears to be a useful endeavor which can be done on a routine basis by many pathologists and one which helps define different groups of patients with differing prognoses.

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Mark Your Calendar

Connecticut State Medical Society
172nd Annual Meeting
April 28, 29, 30, 1964
Statler Hilton Hotel, Hartford

Annual Meeting Of The House Of Delegates
Tuesday, April 28, 1964 — 10:00 A. M.
Statler Hilton Hotel, Hartford

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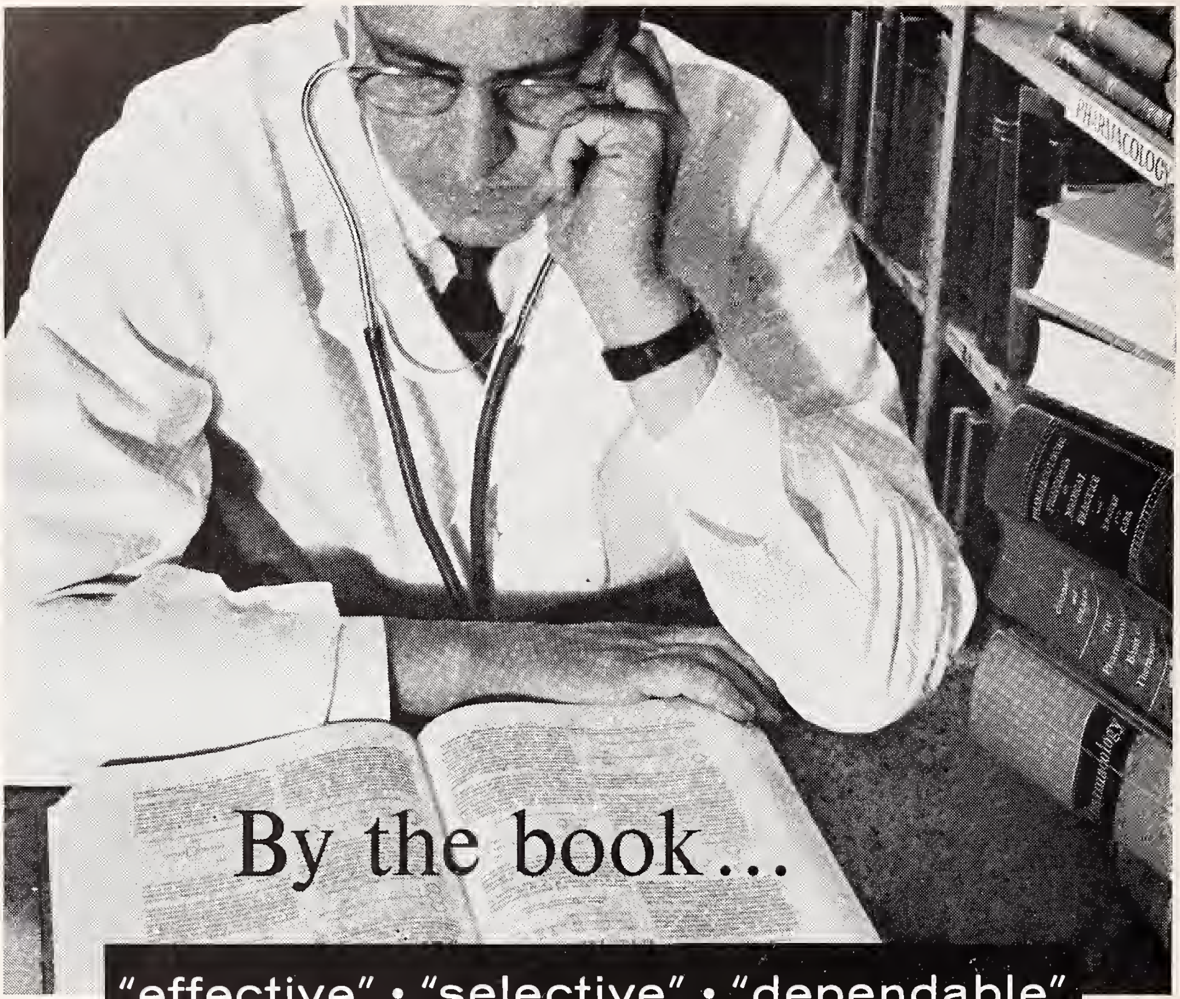

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THE PRESIDENT'S PAGE

Of This And That

On Politics: Do you ever get the feeling you stand alone tilting at windmills? Or is it only because of my exposed position that I find myself screaming into a void in the seemingly futile effort to stem the tide which threatens to overwhelm us. A new administration takes over, Congress reconvenes, and what are the principle items on the agenda?

a. Civil Rights. b. Tax reduction. c. *Medicare under Social Security.*

It seems even a president dedicated to trimming the budget and getting full value for every dollar spent, dedicated to what he calls "frugality," feels impelled to "give away" medical services by Social Security taxation, without seeing any inconsistency in such a stand.

Apparently it does no good to publish data indicating that 67 per cent of 423,000 persons questioned by 32 congressmen in 22 states, during 1963, were opposed to social security taxation to finance medicare. Less than 27 per cent of this large number who responded, favored the proposal, and approximately 6 per cent had no opinion. Yet medicare never seems to lose its tantalizing appeal for the politician.

CSMS vs. CMS: The news is now out. The court's decision upheld CSMS in its contention that CMS acted illegally when it rejected nominees of the Council to sit on the Board of Directors of CMS. The activities of an illegally constituted Board of Directors of CMS during the time of disagreement are likewise illegal, including the June 6th revision of CMS Bylaws. Meanwhile, because of this disagreement, three honorable members of our Society have been kept from performing their designated duties on the Board of Directors of CMS for almost a year. We're pleased it's over. We hope it never happens again. Now let's proceed to make CMS an outstanding service to Connecticut.

On Discrimination: From the AMA House of Delegates Action taken December 4, 1963:

"Resolved, that constituent and component societies having restrictive membership provisions based on race, study this question in the light of prevailing conditions with a view to taking such steps as they may elect to eliminate such restrictive provisions."

In a resolution presented to the House of Delegates as resolution 14, a reference committee recommended it be not adopted. Instead it reaffirms its position adopted in 1950 as expressed in the quote above. Perhaps, symbolic of current social unrest, the decision appears to be less than heroic. Perhaps we find ourselves in a favored position, here in New England, where restrictive provisions have never been a great problem. Such racial restrictive measures have no part in medical organizations, and pussyfooting on the subject is beneath the diginity of our profession.

On Philosophy: I like the following tale of "Frogs and Freedom," which was sent to me along with other interesting material by AAPS,* to whom I wish to give credit:

"There's an old story that says you can't kill a frog by dropping him in boiling water. He reacts so quickly to the sudden heat that he jumps out before he's hurt. But if you put him in cold water and then warm it up gradually, he never decides to jump till it's too late. By then he's cooked!

Men are just as foolish. Take away their freedom overnight, and you've got a violent revolution. But steal it from them gradually under the guise of "security," "peace," or "progress" and you can paralyze an entire generation. Look at the income tax. It started out at a harmless sounding 1 per cent. It would have been easy to jump out of water as tepid as this, but like the frog, we waited while it climbed ever higher (Try jumping now!).

Worst of all, we never learn. Even today we cannot believe that Medicare is the same warm water that will one day boil us in Socialized Medicine. We see no connection between farm price supports and Nationalized Agriculture. And if we draw a parallel between subsidized teachers' pay and federal control of education, we are called "extremist."

The tragedies of history are always repeated by those who refuse to learn them. To seek guidance from the past is not "turning the clock back" as we are so often told. It is merely a good way to keep out of hot water."

Morris P. Pitock, M.D.

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

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160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, January 22, 1964

I. Attendance

Present, in addition to the Chairman, Dr. Martin, were: Drs. Pitock, Gilman, Cullen, Hess, Weise, Sr., Gardner, Wilson, O'Connor, Bradley, Grendon, Grant, Davis, Phillips, Shepard, Weber, Jr., Dean, Ciccarelli, Seigle, Egan, Abbot, Caplan, Spitz, Hastings, and Major. Also present: Mrs. Josephine P. Lindquist, Mr. James G. Burch, Mr. Grant Nickerson (Wiggin and Dana), and William R. Richards, M.D. Absent were: Drs. Goldberg, Scully, Hughes and Gevalt.

II. Routine Business

Approval Of Minutes

It was VOTED to approve the minutes of the meeting of November 21, 1963, as printed and distributed.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Burdette J. Buck, Hartford (HCMA)
Amos E. Friend, Manchester (HCMA)
Richard Karpe, West Hartford (HCMA)
Albert A. Laplume, Florida (HCMA) beginning 1963
Mortimer E. Moriarty, Manchester (HCMA)
Owen L. Murphy, Simsbury (HCMA)
Ralph T. Ogden, Hartford (HCMA)
Maurice F. O'Connell, Hartford (HCMA)
Joseph S. Paladino, Florida (HCMA)
Ernest Rosenthal, Hartford (HCMA)
Charles Russman, Middletown (MCMA)
Raoul A. Siliciano, Bristol (HCMA)

Exemption From Dues

It was VOTED to exempt the following members from payment of CSMS annual dues as follows and for the reasons indicated:

Charles R. Brinkman, III—NHCMA—1963 and 1964—Postgraduate Education.

John A. Muccino – NHCMA – 1964 — Postgraduate Education.

Chairman—Medical Economics Divisional Board

It was VOTED to accept the resignation of Arnold H. Janzen, Hartford, as Chairman of the Medical Economics Divisional Board, and it was further VOTED to appoint Max Caplan, Meriden, to replace Dr. Janzen in this post for the remainder of the current year. Dr. Caplan is a member of the Divisional Board by virtue of his being Chairman of the Committee on Third Party Payments.

Conference Committee With The State Dental Association

Having received assurances from the Chairman of the Dental Association's component of this joint Conference Committee that the Dental Association is anxious to continue this Committee and to reactivate it, it was VOTED to direct the Chairman of the Council to appoint a new chairman of the Society's component to replace William J. Murray, Jr., New London, resigned. Dr. Martin appointed Andrew J. Canzonetti, New Britain, to replace Dr. Murray as chairman for the remainder of the current year.

Resignation—Committee On National Legislation

It was VOTED to accept, with regret, the resignation of Clifford W. Mills, Norwalk, as a member of the Committee on National Legislation. Dr. Mills is also resigning as the FCMA-appointed member of the Committee on State Legislation and will be replaced on that Committee by action of the FCMA Board of Trustees.

County Association Committees On Public Health

In keeping with a resolution filed with the Council by the CSMS Committee on Public Health, it was VOTED to endorse the principles contained in the resolution and notify each component county association of this action. The principles were:

a. That each county association have a standing committee on public health.

b. That such committees be encouraged to become and remain active in studying and acting on matters pertaining to public health in their county areas.

Advisor To State Study Of Chronic Illness

In response to the request of Dr. Ira V. Hiscock, Chairman of the State Health Department's USPHS-sponsored five year study of chronic illness (prevention and treatment) in Connecticut, it was VOTED to direct the Chairman of the Council to appoint a member of the CSMS Committee on Rehabilitation to serve in an advisory capacity to the Study. Dr. Martin appointed Thomas F. Hines, Wallingford, to serve in this capacity. Dr. Hines is Chairman of the CSMS Committee on Rehabilitation.

Ad Hoc Study On Financing Newborn Care

At the request of Albert W. Snoke, New Haven, it was VOTED to direct the Chairman of the Council to appoint two members of the Society to serve with an ad hoc, informal, study group to explore methods of financing medical care of premature and acutely ill newborn infants. Other agencies to participate in this study will be the Connecticut Hospital Association and the State Health Department. Dr. Martin appointed the two CSMS representatives as follows:

Samuel D. Rowley, Hartford (Pediatrician)
Albert L. Larson, Hartford (Insurance)

Student Members

It was VOTED to elect nine medical students to Student Membership in this Society.

Date Of Next Meeting

The Chairman set Thursday, February 20, 1964, as the date of the next meeting of the Council.

III. Old, New And Special Business

Report—Ad Hoc Committee On MAA (Kerr-Mills)

It was VOTED to accept as information a report prepared and filed with the Council by the Ad Hoc Committee on Review of MAA (Kerr-Mills) Program in Connecticut. The report gave detailed information on the performance of Medical Assistance for the Aged which had been furnished by Commissioner Bernard Shapiro and Edwin R. Connors, M.D., Medical Director, State Department of Welfare, at a meeting with the Committee on December 17, 1963.

Report—Ad Hoc Committee On Corporate Practice

Dr. David A. Grendon, Chairman, reported that the question of the legality of the Outpatient Rider being sold by Connecticut Blue Cross had been appealed to the State's Attorney-General for a ruling.

Report—2nd National Congress On Medical Quackery

Max Caplan, Meriden, filed with the Council a detailed report on his attendance at the Second National Congress on Medical Quackery. It was VOTED to accept, with commendation, the report filed by Dr. Caplan. Copies will be distributed to the Advisory Committee on Nutrition and others having special interest in this subject.

Resolutions—P.L. 616

It was VOTED to refer to the Committee on State Legislation, for study and report, two resolutions which had been submitted to the Council by the Committee on Public Health and the Chairman of the Committee on State Legislation respectively. Both resolutions pertained to P.L. 616, which applies to the taking of blood samples for alcohol content determinations from persons arrested for motor vehicle violations in which intoxication is suspected. The motion to refer read as follows: "IT IS MOVED: That Items 12a and 12b of the Council's agenda for the meeting of January 22, 1964 (the two resolutions just described) be referred to the CSMS Committee on State Legislation for study and report to the Council, with recommendations arrived at with the advice of legal counsel, the cost of such legal counsel to be paid for by special appropriation of the general funds of the Society in an amount not to exceed $500.

Directives To The Council—House Of Delegates

1. Concerning a proposed amendment to the Bylaws, Article IV, new Section 7: As directed by the House of Delegates on December 11, 1963, it was VOTED to refer this proposed amendment back to the Council's Subcommittee to Study and Revise the Bylaws for further study and report.
2. Concerning a recommendation of the Report of the Council on Resolution No. 2 (House of Delegates, December 4, 1962): As authorized by the House of Delegates on December 11, 1963, it was VOTED to request the Ad Hoc Committee on Resolution No. 2 to formulate a plan which would provide appropriate prepayment methods for the medical care of the people of Connecticut, and to report its findings to the Council when ready.
3. Concerning an amendment to the Resolution on the Fluoridation of Communal Water Supplies (adopted by the House of Delegates on 12/11/63) which Walter A. Schloss, Hartford, desires to make: It was VOTED to request the Chairman to request Dr. Schloss to furnish the Council with scientific data substantiating the contention

of his proposed amendment, and to suggest that he introduce his amendment at the next (April) meeting of the House of Delegates, perhaps with the endorsement of the Hartford County Medical Association.

Connecticut Medical Service, Inc.

Mr. Grant Nickerson of the law firm of Wiggin and Dana joined the Council during the entire time period devoted to this item on the agenda. Mr. Nickerson advised the Council on a number of matters referrable to the recent decision of the court (which sustained the Society's position on the naming of the physician members and directors of CMS), and counselled the members further on questions pertaining to immediate and future relationships between the two corporations. It was VOTED that all members of the Council were to consider Mr. Nickerson's advice on these matters to be completely confidential.

The Chairman declared the floor open for nominations for four positions as members and directors of CMS, Inc., such named physicians to take office at the Annual Meeting of the Corporation on the third Tuesday of February next. One incumbent, Willard E. Buckley, Middletown, was reported officially as *not* desiring to be re-nominated. The names of the incumbent CMS Members and the physicians named to succeed them are as follows, each post being voted on separately:

Incumbent

Jachin B. Davis, New Haven
Williard E. Buckley, Middletown
Elwood K. Jones, Bridgeport
Francis Gallo, Winsted

Successor

Jachin B. Davis, New Haven
Norman H. Gardner, East Hampton
Elwood K. Jones, Bridgeport
Francis Gallo, Winsted

It was further VOTED to hand-deliver notification of these actions of the Council to the CMS, Inc. administrative offices and this was done on the same day, January 22, 1964. In addition, information copies of the notification were mailed to the four physicians named to take office in February.

In a related action, it was voted to adopt a resolution as follows:

Be It Resolved: That the Council of the Connecticut State Medical Society, through its Chairman, on this date inform the President of CMS, Inc. (in writing) as follows:

1. That the Council holds that the long-standing relationship and working arrangements which have existed between CMS, Inc. and the CSMS since the founding of CMS in 1948 have, in the main, served well to advance Blue Shield in Connecticut to the benefit of the public and of the medical profession, and that, despite occasional differences on admittedly major matters, this relationship and these working arrangements should not now be terminated by either party for any but the gravest and most irreconcilable cause.

2. That, in the Council's opinion, the proposed Amendments to Article I of the CMS Bylaws, if adopted by the Corporation without further liaison discussions, might tend to diminish the confidence of substantial numbers of physicians in the Plan and jeopardize the Plan's effectiveness in continuing to meet the Connecticut public's medical-surgical prepayment needs.

3. That the Council is most willing to discuss reasonable alternative methods by which, in the future, the Society will name the physician Members of CMS, Inc., and to cooperate fully with representatives of the Corporation in seeking to reach mutual agreement on a suitable alternative method, and be it further

Resolved: That the President of CMS, Inc. be urged by the Chairman of the Council to bring these matters to the attention of the Corporators at the convening of their meeting on January 23, 1964, and to request a decision from the CMS Members as to their willingness to discuss these and related subjects with liaison representatives of the Council *before* they move to amend the CMS Bylaws as presently proposed or in any similar manner.

It was further VOTED that thirty copies of this resolution be hand-delivered to the administrative offices of CMS, Inc. and this was done on the same day, January 22, 1964. In a letter of transmittal, the Chairman of the Council requested that the President of CMS, Inc. act in accordance with the intent of the second "RESOLVE" of the resolution. In addition, copies of the resolution were mailed, as information, to all incumbent physician Members of CMS, Inc.

N.B.: *The foregoing is a summary of the proceeding and actions of the Council on January 22, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

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HOUSE OF DELEGATES MEETING — DECEMBER 11, 1963

FURTHER REPORTS OF OFFICERS

Report Of CSMS Delegates To The Annual Meeting Of The American Medical Association

Atlantic City, New Jersey **June 16-20, 1963**

Mr. Speaker, Members of the House of Delegates of the Connecticut State Medical Society, this is a report of some of the actions of the meeting of the American Medical Association House of Delegates in Atlantic City for the 112th Annual Meeting of the American Medical Association from June 16th to 20th, 1963.

This meeting was attended by all your delegates, alternate delegates, your President, General Manager and many members of the Council and the Society. The weather was fine, the city was not as yet too crowded with summer vacationers; the hotel rooms at the Traymore were as ancient as always, but the food was plentiful and good and the New England Hospitality Suite introduced a new cranberry juice concoction which was a tremendous hit with all comers.

Two hundred and twenty-six delegates out of a total of 227 were present for the opening roll call. The business consisted of reports of the four councils of the Board of Trustees, the six Councils of the House, financial statements, award of medals and some sixty-eight resolutions and finally election of officers. This business session lasted for three and one half days. Final registration figures reached a grand total of 36,811 including 12,924 physicians.

The House adopted amendments to the Constitution and By-Laws to increase the size of the *Board of Trustees* from 11 to 15 members, adding three more elected trustees and the immediate past president for a one year term. The new term of office for the Board members is three years with a limit of number of terms to three for a total of nine years maximum service on the Board of Trustees.

The House also decided that *all Section* officers should be elected by members of the Section and that no officers were to be appointed by the A.M.A. Board of Trustees (a real democratic principle which the House usually decides, but sometimes rather belatedly). The House decided as well that —in connection with Section registration—any member desiring to change from one section to another must notify the A.M.A. headquarters of such change at least sixty days in advance of the Annual Meeting.

The House disapproved the Report of the Councils on Medical Service and Medical Education and Hospitals which had recommended that "fees from all sources attributable to services provided by house officers to such patients should be collected for and allocated solely to the financial support of the graduate training programs. " Since there was overwhelming opposition to this recommendation, the House decided "that the A.M.A. record itself as opposed to any system or program by which any part of an intern's or resident's salary is paid out of fees collected by the attending physician or out of fees collected under any type of medical-surgical insurance coverage." The House also recommended that any future proposals on the compensation of house-officers be thoroughly studied by the Law Department and the Judicial Council before submission to the House of Delegates.

In another action related to the controversial "25 per cent rule"—i.e., a hospital to maintain approval of its internship program should have at least 25 per cent of the house staff represented by graduates of American medical schools—the House approved a revision of the *Essentials of An Approved Internship* which deletes the requirement for any stated proportion of foreign medical graduates and graduates of American and Canadian medical schools as an essential feature of any internship program.

The A.M.A.'s Education and Research Foundation received House approval for the establishment of a new *Institute for Biomedical Research,* which will concern itself with intensive and fundamental study of life processes as related to intracellular mechanisms staffed by groups of dedicated, imaginative workers, capable of significant scientific achievements through the interaction of their intellects and experiences, with unmatched facilities and maximum freedom from external pressures, the Institute will do pure, basic, nondisease oriented research and will *not* render medical service to patients *nor* will it conduct a graduate program leading to a degree. The first research group will be functioning by 1965.

An A.M.A. physicians' pension plan, operating along the lines of the Keogh Bill (Public Law 87-792), is planned to be in operation by the end of this year, 1963.

The House is continuing its study on the relationship of *Tobacco and Disease* but emphasizes the duty of the A.M.A. to point out the effects on the young of the use of tobacco and other toxic materials.

The House recommended that local medical societies in the vicinity of medical schools assume the responsibility of establishing and maintaining clear lines of communication with medical students.

The House also approved the organization of the new *National Council for the Accreditation of Nursing Homes,* jointly sponsored by the A.M.A. and the American Nursing Home Association.

Also the House stated that at least one member of the Council on Medical Education and Hospitals, which consists of ten members, shall be a private practitioner of medicine, who is not a faculty member of a medical school nor a member of a staff of a hospital associated with a medical school or university.

Doctor Norman Welch of Boston was elected President-Elect to succeed Dr. Edward Annis in June 1964.

Doctor George Fister of Ogden, Utah, retiring President, told the opening session that "Our fight against federal dictation is not merely one of concern to physicians only and their freedom to practice the best medicine possible, but it also concerns —equally or more so—the individual citizen, all professions and the private enterprise system in this country."

Doctor Edward Annis, in assuming the presidency, stated the importance of maintaining an attitude of individualism among the physicians of America, and urged members of the profession to have courage and individuality to fight for all political, economic and professional freedoms.

Another highlight was the presentation of the Distinguished Service Award to Doctor Lester Dragstedt who is known for his orginal work on gastric physiology, and the Scientific Achievement Award to Doctor John Enders for his work in virology.

All in all the business meeting was very educational and points out the relatively small amount of its energies that the A.M.A. expends in national legislation compared to the tremendous effort it exerts to improve all aspects of the nation's health.

Respectfully submitted,

James R. Cullen, M.D.
Norman H. Gardner, M.D.
Ellwood C. Weise, Sr., M.D.
Delegates to the A.M.A.

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Health Careers Report

On November 14, 1963, Mrs. Allen and Mrs. Chace attended a State Health Careers Committee Meeting at the Connecticut State Medical Society Office in New Haven with Dr. Bernard Mann presiding.

It was discussed at this meeting that we in Connecticut have reached the "crossroads" in our Health Careers program. We must now expand our horizons and obtain the assistance of other participating agencies, such as the Connecticut Hospital Association, Heart Association, the Cancer Society and others who are members of the National Health Council. To accomplish this we must have office space and paid help. The possibility of interesting a large insurance company in helping us finance this program is being explored.

Mrs. Allen conducted the Connecticut Hospital Association Auxiliary Workshop on "Health Careers" on November 19, 1963, at the Waverly Inn, Cheshire. Mrs. Martha Johnson, Public Relations Director of St. Francis Hospital in Hartford, was the chairman, and Mrs. Allen served as the discussion leader on the topic of "Planning A Careers Program." An interested group from 41 hospitals throughout the state attended this workshop.

Mrs. Allen attended the first Eastern Regional Conference on Health Careers in East Brunswick, New Jersey, on December 4 and 5, 1963. This conference was planned by the National Health Council with headquarters in New York City. Mrs. Allen is among the resource personnel who attended this two day meeting. Others who represented Connecticut were: Dr. Max Caplan and Dr. Harold Stern—discussion leaders; Mr. Stanley Katz and Mr. James Burch—recorders; Dr. Bernard Mann and Dr. Edward Breakell—alternate leaders, resource advisors and recorders.

County Facts

Scholarship awards of over $3,000 have been made to eight boys and two girls in medical schools by Hartford County for the current year.

Middlesex County has awarded a scholarship to Linda Carter who is a medical technology student, training at Middlesex Memorial Hospital.

New London County is sponsoring a production of "Rebecca" by the Southington Players to be given at the Masonic Temple in Norwich on January 18th for the benefit of their scholarship fund.

The film "A Cry For Help" was shown to auxiliary members by the Mental Health Committee in the auditorium of the Institute of Living at Hartford on Tuesday, January 14th. Dr. Raymond Veeder, Clinical Director of the Institute, discussed the film and conducted a question and answer period. This film was shown as part of the suicide prevention program of the AMA as outlined by Mrs. Robert L. Garrard, National Mental Health Chairman.

The annual Medi-Capers dance of the Hartford County Auxiliary for the benefit of their scholarship fund was held on January 18th. The Happy and Food Tasting Fair sponsored by the New Haven County Auxiliary was a successful venture both socially and financially. Benefits were added to the scholarship funds.

Our representative to the Connecticut Advisory School Health Council, Mrs. Dewey Katz, reports that this Council is studying suggested means of extending and improving health plans in the Connecticut school system. Reports from the Council indicate that more health education courses are needed in the schools.

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Arthralgen is especially useful for the prompt relief of early morning stiffness and pain with less risk of gastric irritation. And since Arthralgen contains no sodium it is safe for long-term use in arthritics who have other conditions which nece sitate sodium restriction.

ARTHRALGEN®-PR

Each tablet contains:

Salicylamide	250 m
Acetaminophen	250 m
Ascorbic acid (Vitamin C)	25 m
Prednisone	1 m

The basic Arthralgen formulation plus predr sone is indicated for patients who require steroi Prednisone has three advantages over cortiso hydrocortisone, and ACTH. They are: (1) lack sodium retention, (2) absence of increased pot sium excretion, and (3) the unlikelihood of stero induced hypertension.*

BRIEF SUMMARY

Arthralgen and Arthralgen-PR are indicated the management of rheumatoid arthritis, acu

rthritic joints from

I

N

uty arthritis, rheumatoid spondylitis, osteoar-
itis, bursitis, fibrositis, and neuritis. Arthralgen
y be used for analgesia in colds, flu, and
rious myalgias.

SAGE: One or two tablets four times a day.
ter remission of symptoms, dosage should be
luced to the minimum maintenance level.

DE EFFECTS: Nausea, GI upset, or mild salicy-
m may rarely occur. Symptoms of hypercorticoid-
n dictate reduction of dosage of Arthralgen-PR.

ECAUTION: Reduction in dosage of Arthral-
n-PR given over a long period should be gradual,
ver abrupt.

NTRAINDICATIONS: Hypersensitivity to any
gredient.

s with any drug containing prednisone, Arthral-
n-PR is contraindicated, or should be administered only with care, to patients with peptic ulcer, tuberculosis, nephritis, diabetes mellitus, acute psychoses, Cushing's syndrome (or Cushing's disease), overwhelming spreading (systemic) infection, or predisposition to thrombophlebitis.

Arthralgen-PR is generally contraindicated in patients with uremia and viral infections, including poliomyelitis, vaccinia, ocular herpes simplex, and fungus infections of the eye. It is also contraindicated in patients with chicken pox or susceptible persons exposed to it.

SUPPLY: Arthralgen (white, scored) and Arthralgen-PR (yellow, scored) tablets are available in bottles of 100 and 500.

*Cohen, et al: J.A.M.A., 165:225, 1957.

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1964 MEETINGS

March 19 – 180th Annual Meeting of the New Haven County Medical Association will be held at Waverly Inn, Cheshire, Conn. Business Meeting scheduled for 2:30 P.M.

April 28-30—Annual Meeting Connecticut State Medical Society, to be held at Statler-Hilton Hotel, Hartford.

May 25-27—Annual Meeting American Thoracic Society Medical Section of the National Tuberculosis Association to be held in New York City.

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

Winifred L. Mroz, age 34—M.D. Bonn Germany, 1956. Internship White Plains, N. Y. 4 years. Interested in Obstetrics-Gynecology. Available July 1, 1964.

David H. Steinberg, age 31—M.D. State University of N. Y. 1959. Interested in Internal Medicine and Cardiology. Available July 1964.

PLACEMENT OPPORTUNITIES

INDUSTRIAL PHYSICIAN—for state employees' clinic located in Hartford. 35 hour week, 3 weeks vacation, up to 120 days sick leave, paid insurance program, social security and liberal retirement. Requires at least two year's general practice. Salary range $11,100-$15,080. Reply to B. Dearington, State Department of Health, State Office Building.

State of Connecticut desires to fill a position for a physician in a State Training School and Hospital.

Hartford County is in need of a physician in town of 19,000 persons.

New London County needs a general practitioner.

Physician and internist available in the near future in combined tuberculosis and chronic disease hospital.

ANYONE INTERESTED IN "PLACEMENT WANTED" AND "PLACEMENT OPPORTUNITIES" IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN ST., NEW HAVEN.

In Memoriam

Apsel, Abraham, died in Bridgeport on January 9, 1964. Born in New York City June 6, 1891, Dr. Apsel, a urologist, received a degree in pharmacy from the Brooklyn College of Pharmacy in 1913 and was graduated from Long Island College Hospital in 1918. In the same year, he began a year internship at St. Vincent's Hospital, Bridgeport, and was licensed to practice in December, 1918.

Dr. Apsel served a three year residency at St. Vincent's and in 1933 received a Master of Science degree in urology from the Graduate School of the University of Pennsylvania School of Medicine.

He was elected to membership in the Fairfield County Medical Association and Connecticut State Medical Society in 1920 and was a member of the Section on Urology of the State Society. He had served as attending urologist at St. Vincent's Hospital.

Lynch, Hubbard, Bridgeport; New York University and Bellevue Hospital Medical College, 1924. Dr. Lynch was a Quartermaster First Class in the United States Naval Reserve Force from July 19, 1918 to December 22, 1918. He was on the Courtesy Staff at the Bridgeport Hospital. Dr. Lynch was a member of the International Academy of Proctology, the New York Academy of Medicine, the American Medical Association, the Fairfield County Medical Association, and the Connecticut State Medical Society. Dr. Lynch died December 28, 1963, at the age of 65.

O'Brien, Francis J., Bridgeport general practitioner died on January 14, 1964. Dr. O'Brien was born in Ansonia, March 22, 1892. He attended Holy Cross College in Worcester and was graduated from Fordham University School of Medicine in 1917. He served an interneship at St. Catherine's Hospital, Brooklyn. He served in the U.S. Navy from April 6, 1917 to May 6, 1919. Licensed in Connecticut in 1920, he was first elected to membership in the Fairfield County Medical Association and Connecticut State Medical Society on October 13, 1925. He was attached to St. Vincent's Hospital, Bridgeport.

Doctor's Office

Peter V. C. Dingman, M.D., and James M. Cary, M.D., announces the removal of their offices from 155 Grove Street to 1211 West Main Street, Waterbury.

Jerome M. Hopper, M.D., announces the opening of an office for the general practice of medicine on Church Street in Windsor Locks.

Robert B. Hurowitz, M.D., announces the opening of an office for the practice of pediatrics at 369 Main Street, West Haven.

Henry J. Sharon, M.D., announces the opening of an office for the practice of general surgery at 201 Main Street, New Britain.

John E. Standard, M.D., announces the removal of his office from 159 Meadow Street, Naugatuck to 1211 West Main Street, Waterbury.

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MEDICAL OFFICE SUITE available for rent in West Haven, Connecticut, population 45,000, ideal central location, ground floor; near hospitals. Excellent opportunity, urgent need for a surgeon, ophthalmologist, obstetrician, pediatrician, psychiatrist and chiropodist. Reasonable rent includes heat. Please write or telephone Jacquin D. Phillips, 319 Juniper Drive, Orange, Connecticut, Dial 387-4138.

CLINTON, CONNECTICUT. Home built by a physician. Lower level used as office with 3 rooms and 2 powder rooms. Second level has 4 rooms and bath. Third floor expansion. Hot water baseboard heat. Price: $25,000.00. Norman R. Foerch Agency, Phone: MOntrose 9-2000 or 9-8922.

W. B. SAUNDERS COMPANY features the following new books and new editions in their full page advertisement appearing elsewhere in this issue:

1964 CURRENT THERAPY VOLUME
New!—Today's best treatments—ranging from updated information on general immunization to newer agents in Rx of meningitis.

BOCKUS—GASTROENTEROLOGY
New (2nd) Edition!—An eminent 3-volume work. Covers all known primary and secondary disorders of the digestive tract and its appendages.

REUTER—ATLAS OF UROLOGIC ENDOSCOPY
New!—Explains in word and picture precisely how to use the endoscope.

Letter To The Editor

To the Editor,

Dr. Daniel P. Griffin can hardly escape the suspicion of having (Conecticut Medicine 27: 645 [Oct.] 1963) thought that "It gave me furiously to think"—or, in his father's "rusty French," "il m'a donné furieusement à penser"—means "It made me think very hard." It doesn't. It means "It puzzled me."

Sincerely yours,
HENRY L. ARNOLD, JR., M.D.

Honolulu, Hawaii

P.S. My warmest compliments on a fascinating treatment in depth of such an important topic; I read it with such care and attention that I was even rewarded with a passing chuckle when I encountered (p. 626) the "Delhi oracle"—an Indian substitute for the usual Greek one, on doubt!

Special Notices

INTERNATIONAL ACADEMY OF PROCTOLOGY
February 29-March 5, 1964

International Academy of Proctology Sixteenth Annual Teaching Seminar, Deauville Hotel, Miami Beach, Florida, February 29-March 5, 1964, Jacob Reichert, M.D., President; and Donald C. Collins, M.D., General Convention and Program Chairman.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

The Nature of Biochemistry by Ernest Baldwin, Ph.D., Cambridge at the University Press, 1962, 111 pp. $1.45.

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The discharged
mental patient . . .
and Thorazine®
brand of chlorpromazine

"The average practitioner is quite capable of handling the vast majority of ex-institutionalized patients by regulation of medication, reassurance, manipulation of the environment where necessary, and . . . other technics." Kline, N.S.: Postgrad. Med. 27:620 (May) 1960.

The family physician must often assume responsibility for the discharged mental patient. Thorazine (chlorpromazine, SK&F) can be a valuable adjunct to the continuing care of this patient, because it helps prevent relapses by insulating him from the impact of stressful experiences. For successful rehabilitation and prevention of rehospitalization, however, the former mental patient—and often his family—also needs the guidance and counsel of his physician.

Many physicians are surprised by the high doses of Thorazine (chlorpromazine, SK&F) used in patients released to their care from mental hospitals. This surprise may be expressed by a drastic reduction in dosage "to play it safe"—with serious consequences for the patient.

The successful maintenance of former mental patients requires adequate, often "high" dosage, and often for prolonged periods of time. Fortunately, these dosages do not mean greater risks for the patient. On the contrary, there is much less risk of serious side effects once a patient has become gradually accustomed to Thorazine (chlorpromazine, SK&F)—*regardless of dosage*—over a period of a few months. Continuing therapy is almost always well tolerated, and is essential to most patients' continued well-being.

Brief Summary: Thorazine (chlorpromazine, SK&F) has been successfully used for 10 years in the treatment of mental and emotional disturbances, and has proven highly effective in the maintenance therapy of former hospitalized mental patients. *Principal side effects:* The most frequently encountered side effect is transitory drowsiness. Other occasional side effects include: dry mouth, nasal congestion, constipation, miosis, dermatological reactions, photosensitivity, jaundice, hypotension, increased appetite and weight; very rarely, mydriasis, agranulocytosis, extrapyramidal symptoms. *Contraindications:* Comatose states or in the presence of excessive amounts of C.N.S. depressants.

For complete prescribing information, please see *PDR* or available literature.

SK&F *Smith Kline & French Laboratories*

NEW BOOKS IN REVIEW

MARGIN OF SAFETY by John Rowan Wilson, Doubleday & Co., Inc., New York, New York, 1963, 258 pp., $4.95.

Reviewed by: GERALD I. PITEGOFF

There are certain areas of human endeavor where we expect an exactness equilibrated with factual reality. Science has been regarded as a realm of mathematical formulae and chemical equations detached from bias and emotionalism. However, it is important that we recognize that although science may be high in an ivory tower, the scientist is competitive, emotional and subject to environmental influences.

The author has undertaken to tell the story of the development of the Salk vaccine and the prevention of poliomyelitis. The story proceeds with a quality of mystery even though it is a familiar one to the medical profession. The failures, frustrations and the ballyhoo that accompanied the scientific investigations are presented in a clear and simple style—albeit cynical. Included in the book is a chronological table of the year to year developments. An introduction serves as an essay on the American attitude—"We can do it as long as we have the money and the publicity."

Dr. Wilson ably develops the story of man's attack on disease beginning with Jenner's work with smallpox, Pasteur's investigations and Koch's postulates for scientific knowledge. With this background establishing immunization as a weapon of medical prophylaxis, the position of poliomyelitis in its relative position as a scourge of mankind is presented. It is a relatively rare disease but the results leave their imprint on the memory of all who see them. However, until the disease afflicted the leader of a great nation, it was of interest only to scientist and patient. It now became big business with The National Foundation for Infantile Paralysis under the leadership of Basil O'Connor promising conquest of the disease. Paradoxically, the disease attacked the richest nation in the world with the most advanced sanitation and hygiene, specifically because of these selfsame conditions. With poverty, squalor and filth an immunity could be developed by the time the individual attained adulthood.

While the story of the prevention of polio has been a gratifying triumph, the attempts at treatment have been frustrating and unsuccessful. Dr. Edward Schultz of Stamford University undertook to screen various substances which, when sprayed in the nostrils, would protect the body from the entrance of the polio virus. It was believed at that time that the polio virus entered the body through the nose and via the olfactory nerves, made its way to the spinal cord. Using Schultz' zinc sulphate solution, trials on thousands of children in Toronto and Alabama were carried out with resultant discomfiture and little success. Dr. Retan then suggested the heroic measure of washing the virus out of the nervous system with saline. Fortunately, Dr. S. D. Kramer tested the routine on monkeys. The results were disastrous.

Virologists by 1934 were convinced that the use of a vaccine offered the only hope of conquering polio. Dr. William H. Park of the New York City Health Department, with the assistance of Maurice Brodie, developed a killed virus vaccine.

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Pentaerythritol tetranitrate may infrequently cause nausea and mild headache, usually transient. Slight drowsiness may occur with meprobamate and, rarely, allergic reactions. Meprobamate may increase effects of excessive alcohol. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction. Like all nitrate-containing drugs, 'Miltrate' should be given with caution in glaucoma.

Dosage: 1 or 2 tablets *before meals* and at bedtime. Individualization required.
Supplied: Bottles of 50 tablets.

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meprobamate 200 mg.+
pentaerythritol tetranitrate 10 mg.

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A few days later, Dr. John A. Kolmer of the Institute of Cutaneous Research of Philadelphia announced that he too had an attenuated live vaccine. The Kolmer-Brodie vaccines, despite assurances of safety, resulted in a complete fiasco with Leake reporting the incidence of paralysis in the Journal of the American Medical Association in 1935. Research in polio was minimal until 1949 when John Enders reported his success in growing the polio virus in tissue culture. In the same year, Dr. David Bodian and his associates at Johns Hopkins demonstrated that there are three separate types of polio virus each producing its own specific antibodies. By 1952 Dr. Bodian and Dr. Dorothy M. Horstmann presented proof that the transmission of the polio virus was not up the nerve pathways. It was now evident that the production of antibodies in the blood could effectively protect against the polio virus. The stage was now set for the battle of the killed virus versus the live vaccine.

Dr. Jonas Salk, protege of Dr. Thomas Francis, Jr., financed, encouraged and publicly followed by the National Foundation pushed on to develop a killed vaccine. Drs. Cox and Koprowski financed by the Lederle Laboratories, American Cyanamid Company, bent all efforts to develop an attenuated live vaccine; and Dr. Albert B. Sabin, working at the University of Cincinnati, also was eager to develop an attenuated live vaccine. The race was won by Dr. Salk with the results being announced in a truly theatrical demonstration employing the most unscientific behavior. The unfortunate abdication of the U. S. Public Health Service to the National Foundation then resulted in confusion and disenchantment. The Cutter Vaccine disaster almost threatened to wreck the entire polio vaccine program. However, Cox, Koprowski and Sabin now pushed on with their investigations seeking new fields to test their product. Sabin turned to the Soviet Union and became the victorious hero with an effective attenuated live vaccine.

The book concludes with an essay on a look at the future enriched by our scientific knowledge, profiting from the experience of the past decade with polio research. Significantly, the author states that perhaps we can look forward to the day when, "One of the most important criteria by which nations will be judged will be their management of the advances of science."

For the scholar and student the book has a fine index and list of source material. It is a book that will reward both the physician and layman who permit themselves the delight of reading it.

THE THYROID AND ITS DISEASES, 3rd Edition by James H. Means, M.D., Leslie J. DeGroot, M.D., and John B. Stanbury, M.D., with a chapter on Surgery of the Thyroid by Oliver Cope, M.D., McGraw-Hill Book Company, Inc., New York, 1963, 618 pp., $15.95.

Reviewed by: PAUL H. LAVIETES

The reviewer recalls vividly the excitement which the first edition of this book provoked in him in 1937. As stated in the author's preface it was in no sense an encyclopedic treatise but rather an account of the personal experiences of a group of workers in a single clinic and of the opinions and convictions derived from this experience. Because the clinical material available to the group was rich, most clinically

reduce or obviate the need for transfusions and their attendant dangers

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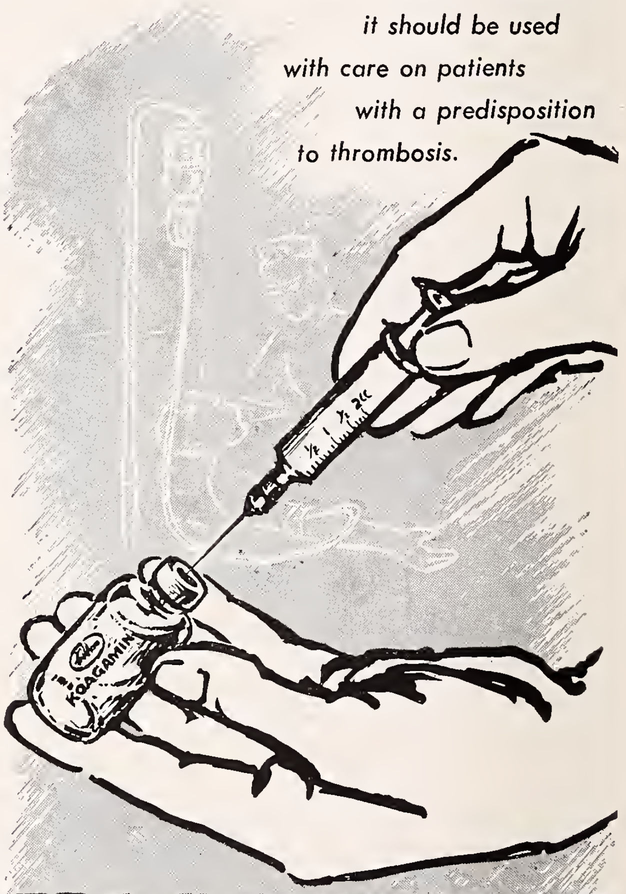

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pain *is almost invariably a presenting symptom in cases of skeletal muscle* *spasm*

In some instances, the pain subsides on relaxation of the muscles in spasm. In others, relaxant therapy alone fails to give adequate relief, and supplementary analgesia (and possibly sedation) are indispensable, as in cases of:

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severe pain, when the degree of pain is such as to cause persistence of symptoms in spite of relaxant therapy.

emotionally aggravated pain, when anxiety or agitation creates tension that thwarts the efficacy of both relaxant and analgesic medication.

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Phenobarbital (⅛ gr.)....8.1 mg.
(Warning: May be habit forming)

ROBAXISAL and ROBAXISAL-PH are indicated in strains and sprains, painful disorders of the back, "whiplash" injury, myositis, pain and spasm associated with arthritis, torticollis, and headache associated with muscular tension.

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Contraindicated for patients hypersensitive to any component of the formulations. There are no specific contraindications to methocarbamol, and untoward reactions are not to be expected.

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liquefying secretions in the
spiratory tree, Cheracol makes it easier
the patient to cough—in accord
h the physiologic defense mechanism.

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important subjects were covered. The book had the authority that comes with the experience of superb clinicians who strove always to rest diagnosis and treatment squarely on scientific understanding. Since it made no pretense of being encyclopedic, the bibliography was not comprehensive, but critical and selective. It stood out in the reviewer's mind as the best book on thyroid disease and a model of medical writing.

Since then new techniques have greatly extended our knowledge of the thyroid and much of this has found application to diagnosis and therapy in thyroid disease. During this time, members of the clinic have been major contributors and many have moved on to continue the tradition throughout the world.

The new edition, like its predecessors is primarily clinical, with a strong foundation in anatomy (including a fascinating section on phylogeny and ontogeny) and physiology. The chapter on diagnostic techniques begins characteristically with a useful discussion of the history and physical examination and only then proceeds to describe the many laboratory tests and what to expect from them. The authors state that if the tests are not in accord with one another or if they fail to support the clinical impression in any case, clinical judgment and time are likely to resolve the dilemma, that blind adherence to laboratory determinations may prove disastrous.

In discussing the clinical disease entities, the orientation is again primarily clinical with a strong foundation in investigative work. There is much that is new since the 2nd edition, for example a discussion of the risk of carcinogenesis from treatment with radioactive iodine, the use of synthetic levothyroxine and triiodothyronine in hypothyroidism, the extensive new studies on endemic goiter with hypothyroidism, and the extensive new knowledge in relation to thyroiditis and to nodules and neoplasms. Finally there is an excellent section on surgery by Oliver Cope.

Despite the great complexity of the subject matter, the authors have succeeded in maintaining the clarity and homogeneity of the first edition. Illustrative case records are again used to good effect and the bibliography, while of course more extensive than previously, gains by selectivity. This is a book to be treasured by the clinician and the investigator alike.

CARDIOVASCULAR SURGERY 1962, Proceedings of the Council Cardiovascular Surgery, American Heart Association, Monograph No. 6, Edited by John M. Howard, American Heart Association, New York, 1963, $3.00.

Reviewed by: LOUIS H. NAHUM

A glance at this issue shows how far we have gone in fifteen years. Surgeons are now in the forefront of theoretical and practical advances made in the laboratory, operating room and bedside. When we see that this issue contains forty-one articles and 127 contributors, it is clear that the cardiovascular surgeons are working as part of a multidisciplinary investigative and clinical team. The fact that this section of circulation was sponsored by the American Heart Association reveals that internists no longer dominate this great group but surgeons are entering in increasing numbers to advance the ideals for which the American Heart Association was set up. As Professor Howard states in his foreword "Surgery and the American Heart Association have much to offer to each other."

The subjects treated are virtually every aspect of cardiovascular surgery. New operations for patent ductus, aortic aneurysms, establishing a collateral coronary circulation. New techniques to avoid dangers and pitfalls of cardiopulmonary bypass. Studies on anastomosis of superior vena cava and pulmonary artery. New methods of correcting Tetralogy of Fallot. Correcting aortico-left ventricular tunnel. Then there are papers on new aortic valves, flexible vascular adhesive, suturless heart valves and implanted pace-makers. There are also papers on basic science such as auto-transplantation of the canine heart, control of severe acid base balance; intravenous mannitol in obiguria, hypoxia and arrhythemia, electron microscopic studies of myocardial actomyosin, changes in hemorrhagic shock treated by hyperbaric oxygenation. There is a paper on an artificial placenta and one on assisted circulation to the left ventricle and others.

Clearly here we have a panoramic view of cardiovascular surgery in the U.S.A. in 1962. There are no papers from abroad and therefore the title is somewhat misleading since it assumes that progress in the U.S.A. is the total progress. Aside from this perhaps unjustified self-sufficiency, these proceedings are a landmark and should be read by all those interested in heart disease.

MODERN CLINICAL PSYCHIATRY, Sixth Edition by Arthur P. Noyes, M.D. and Lawrence C. Kolb, M.D., W. B. Saunders Co., Philadelphia, Pa., 1963, 586 pp., $8.00.

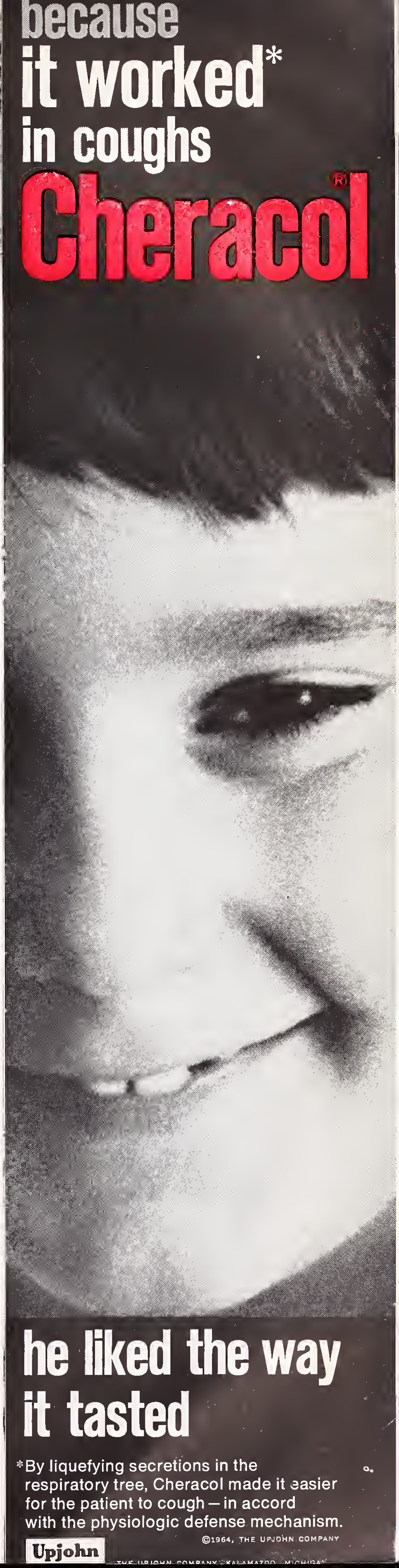
Reviewed by: LOUIS H. NAHUM

In this excellently printed book one will find a brief but clear and precise treatment of Modern Clinical Psychiatry. The authors are authoritative in their field and have incorporated in this Sixth Edition the vast amount of new learning and knowledge that pertains to personality, its development, and pathology. This necessitated a considerable revision and reorganization of earlier chapters. The consequences of deprivation of all kinds upon growth and later integrative functions of the personality, derived from studies of social isolation and various laboratory investigations are included.

New sections on brain syndromes, Wilson's disease, ammonia poisoning in hepatic insufficiency, headache and gastrointestinal disorders are also included, so are chromosome abnormalities in mongolism, specific metabolic defects of enzymes that lead to defective brain growth and intellectual retardation. So also we find the clinical successes of new antidepressant agents.

A brief excellent objective coverage of the various forms of psychotherapy is found in a chapter on psychotherapy. Personality development, child psychiatry, shock therapy are all excellently treated. There is a final chapter on psychiatry and the law which could be read with benefit by doctors, lawyers, judges and social workers.

This book of thirty-five chapters with historical development and an excellent index with over 100 new items reflects the scholarship of the authors and the up-to-date treatment of the subject. It is an excellent reference book for students, internes, physicians, lawyers and social workers.



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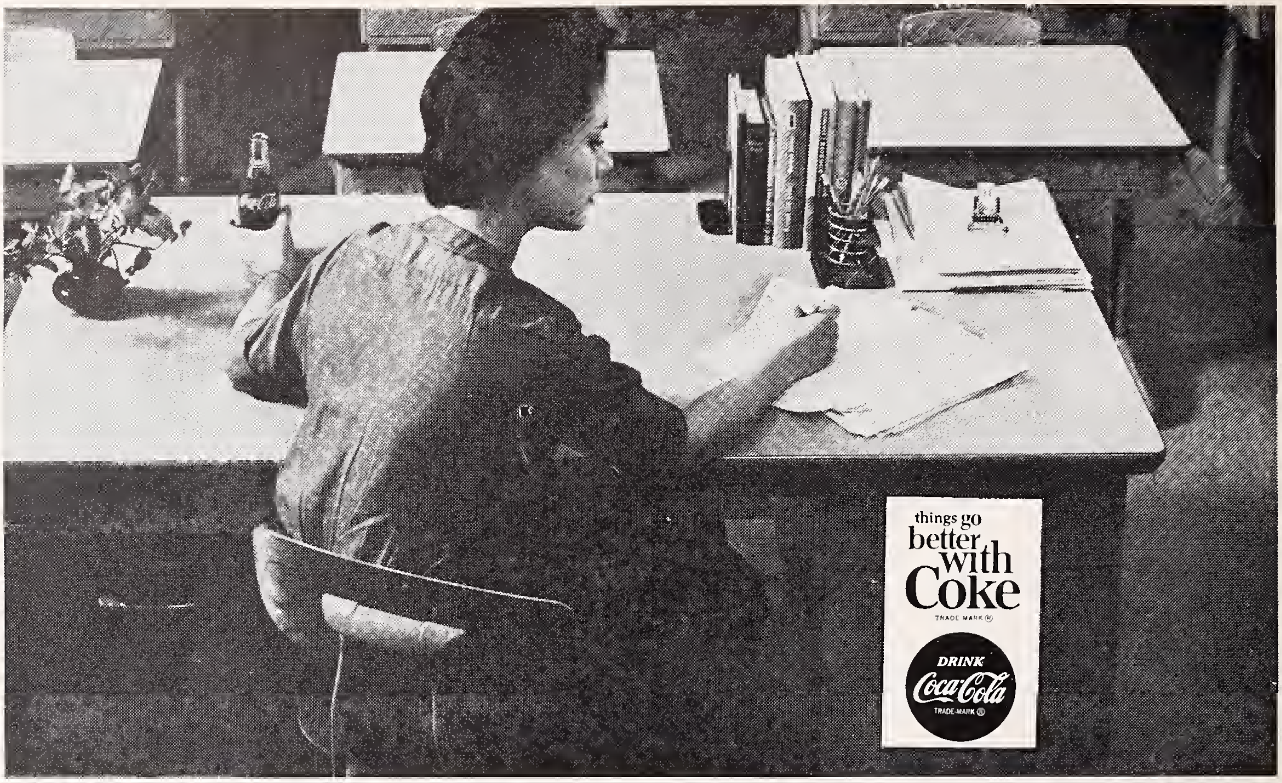

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Connecticut Medicine

Connecticut State
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Volume 28 / March 1964 / Number 3

Medical Aspects Of Nuclear Warfare: I—Marshall Brucer, M.D., *Guest Editor*

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HELMHOLTZ: PHYSICIST-PHYSICIAN (see page 151)

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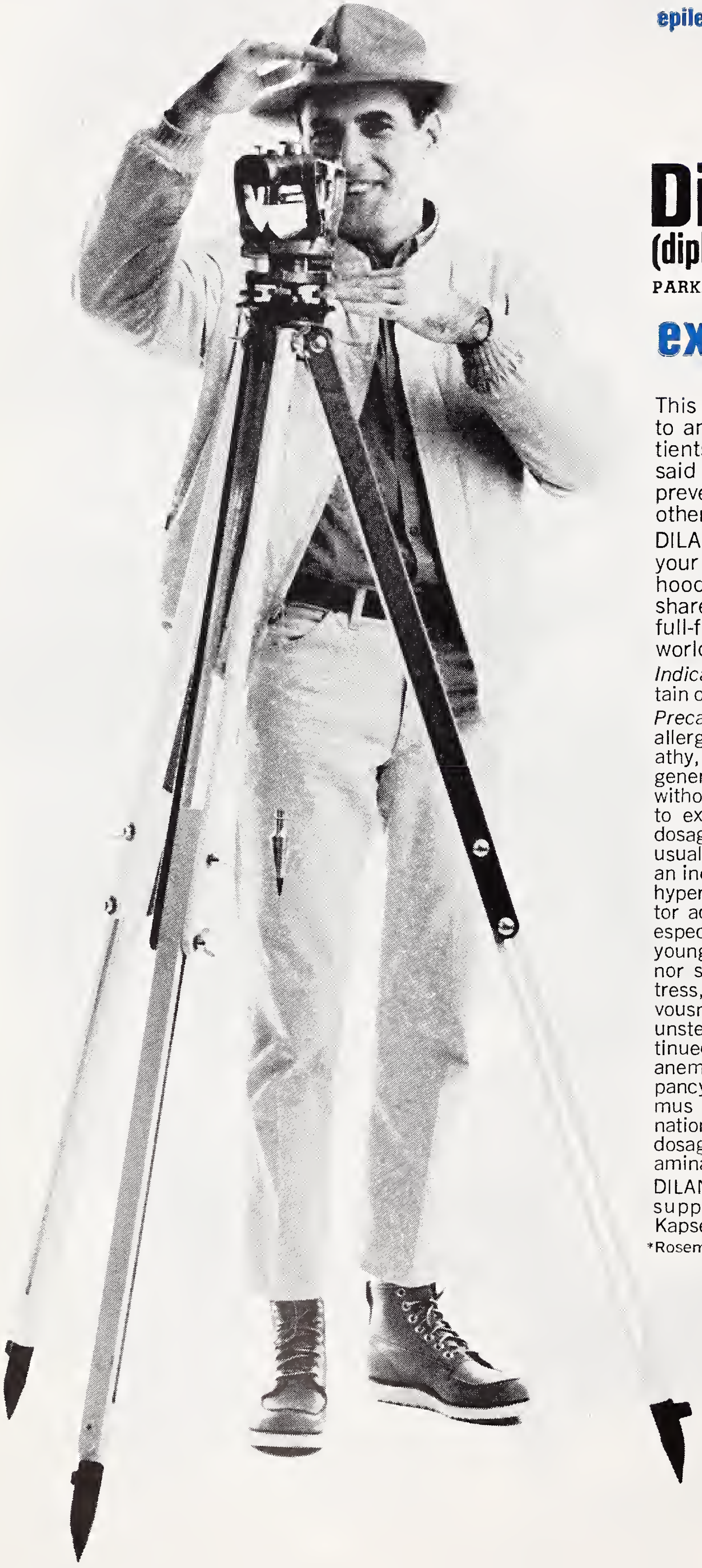

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*Roseman, E.: *Neurology* **11**:912, 1961. 33664

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The Guest Editor

Dr. Marshall Brucer our Guest Editor for this outstanding contribution on "Medical Aspects of Nuclear Warfare" went from a study of philosophy to physics to physiology and medicine.

He taught physiology at the University of Texas. At Oak Ridge Institute of Nuclear Studies he learned how to use and not to use isotopes. While at Oak Ridge he unfortunately developed multiple sclerosis. In spite of this handicap, Dr. Brucer has carried out prodigious work. He has written numerous articles on atomic physics and medicine. His special memberships, consultantships and appointments are:

National Committee on Radiation Protection, Subcommittee 9, 1951-

National Academy of Sciences—National Research Council, Committee on Radiology, 1957-

Picker Foundation Subcommittee, 1957-

Technical Advisor on Damon Runyon Committee, 1952-1953

Trustee, Tennessee Chapter, American Cancer Society, 1952-1955

Medical Advisor, Tennessee Chapter, National Multiple Sclerosis Society, 1961-

AIBS, College Visiting Biologists Program, 1960-

MEND Visiting Lecturer Program, 1960-

Local Lecturer, Sigma Chi, Nu Sigma Nu, Alpha Omega Alpha, many medical societies, 1952-

Consultant, Surgeon General, USAF, 1954-1957

Consultant, Armed Forces Institute of Pathology, 1957-

Consultant, Department of Defense, 1960-

Consultant, Surgeon General, USA, 1960-

American Society for Testing Materials Committee B9, Subcommittee III-E

Oak Ridge Traveling Lecture Program, 1952-

Dr. Brucer's productivity is an excellent example of what Penfield calls the "second career." He is at present Chairman of the Committee on Scientific Program 1964 of The Society of Nuclear Medicine.

L.H.N.

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editorials

The Blueprints Of Life's Architecture

Advances are coming so fast in genetics, that a real understanding of the most intimate nature of life may not be far off. Much about basic genetic mechanisms have been learned from microorganisms, bacteria, viruses and microscopic plants, because these things multiply in huge numbers and in a very short time, so that they can be crossed and otherwise manipulated experimentally. It is now generally agreed the information necessary for the complete functioning of the living cell is contained within the deoxyribonucleic acids (DNA) —that constitutes the chromosomes of the cell which reside in the nucleus. It is believed that a single DNA molecule is responsible for each function which the cell must perform, and that each DNA is different from all the others. All true growth is by cell division during which each DNA molecule replicates itself, one going to each daughter cell as a part of the chromosome structure of the nucleus.

The life of an animal starts from a fertilized cell and as the embryo developes, cells become specialized into liver cells, kidney cells, brain cells, etc., each performing different functions. The DNA molecules are thought to regulate the various functions of each cell through complex reactions involving an intermediate set of molecules the ribonucleic acids (RNA). Presumably each DNA molecule can synthesize its corresponding RNA molecule, which then diffuses out of the nucleus into the cell cytoplasm where it is responsible for the synthesis of a particular enzyme. All cells in the body are thought to be potentially capable of performing the function of all cells. In the highly differentiated cells, however, some cell functions are accentuated while others are suppressed. This, of course, means that a cell like the neuron must have a great many DNA molecules in its nucleus which are never used.

It is believed that for each functional DNA molecule there are at any one time a great many corresponding RNA molecules which are constantly being synthesized by the DNA. The RNA molecules in turn synthesize even more corresponding numbers of protein molecules. Presumably there are feedback mechanisms which regulate those synthetic processes to maintain a dynamic equilibrium for each cell. Less than three years ago, a research team at the National Institute of Health broke the genetic coding mystery and showed how hereditary information contained in DNA becomes translated into the synthesis of the protein molecules of the cell. It should be remembered however, that while DNA can replicate itself, RNA cannot. Accordingly a cell with only RNA cannot continue to function for any length of time.

Mammalian red blood cells function but a few weeks without a nucleus. When a sea urchin egg is centrifuged into two halves, a nucleate and non-nucleate fraction the "cell" lacking a nucleus undergoes cell division for a few times only, and then dies. Mammalian tissue culture cells that have had their DNA damaged by radiation will divide a few times then become bizarre and die. Unless DNA is

THE COVER

HELMHOLTZ: PHYSICIST-PHYSICIAN

AMONG great contributions to medicine in the nineteenth century was the ophthalmoscope, an instrument used for inspection of the interior of the eye, invented in 1850 by Hermann Ludwig Ferdinand von Helmholtz (1821-1894), Professor of Physiology at Königsberg. Physician by training and teacher by profession, Helmholtz became Germany's foremost physicist, succeeding to the Chair of Physics at the University of Berlin. His contributions to medicine's knowledge of acoustics nearly equaled those he made to physiologic optics. His discoveries in physics advanced knowledge in a dozen scientific fields, earned him ennoblement, and brought him eminence, distinction, and world-wide recognition during his life.

actively synthesizing RNA the cell will not long survive. Wulff, Quastler and Sherman found in brain cells, that DNA is essential for the day to day functioning of these cells and that DNA is actively synthesizing RNA. This probably occurs in all other cells as well. If faulty RNA is produced, one can expect synthesis of defective enzymes. This then could be a factor in aging of all non-dividing cells of the body such as brain, muscle, kidney, etc. Since faulty RNA comes from damaged DNA, a study of the factors damaging DNA could throw light on the aging process.

Two factors capable of damaging DNA are now known, nitrogen mustard and radiation. Nitrogen mustard breaks chromosomes in bone marrow cells and intestinal mucosa, but these cells undergo cell division quite rapidly and any damaged chromosomes would be quickly discarded during repeated cell divisions, so that the mutagenic effect would disappear. The agent does not cause damage to the cells which rarely or never undergo cell division, which includes the vast majority of all cells in the body, and therefore it leaves no permanent effect nor does it accelerate the aging process.

Radiation however, is a different mutagenic agent for it produces damage to chromosomes of all body cells, not just to the rapidly dividing ones. It has been known for many years that administration of low-level x- or gamma-radiation over a period of months is only about one-quarter as effective in shortening life as a single administration of high level x- or gamma-radiation. The chromosome aberrations develop rather slowly in mice subjected to long term low-level irradiation whereas a single large dose produces chromosome aberrations plentifully and promptly. On the other hand long term low level neutron irradiation is just as effective in shortening life as large single doses of neutron radiation. These experiments show that a good deal of chromosomal recovery can take place after low-level x-irradiation, but none can occur after low-level neutron radiation. Thus the correlations observed thus far between development of chromosomal aberrations, somatic mutations, and life span are very impressive. Factors either artificial or spontaneous which increase the mutation rate also decrease the life span.[1]

Even without radiation, it is now known that somatic cells of the mammal develop chromosome aberrations spontaneously at fantastically high rates. Some strains of mice exhibit grossly abnormal mitoses in 70 per cent of all liver cells and presumably an equal proportion in all non-dividing cells when mice are hardly past middle age. Surely this must mean that virtually all cells carry many gene mutations, probably more than are observed, because many of the breaks in the chromosomes may have healed before the time of observation. If DNA damage occurs in a non-dividing cell, the organ of which the cell is a part will suffer because the defective cell will function inadequately and its death will be high.

On this basis organs with non-dividing cells should be the ones to accumulate mutations which will cause senescence, while the ones with rapidly dividing cells, if they are well supported should be immortal. This appears to be the case in the blood forming organs which are constantly replicating themselves and function well into old age, whereas the muscle cell which does not replicate itself is one of the first to show weakness as a sign of advancing years. This is also true of the brain which has been estimated to lose without replacement about 10,000 brain cells every day. It is small wonder that mental ability decreases after some decades.

One lesson from this adventure into genetics is, that if we wish to slow down the aging process, we must at all costs reduce hazards of radiation, whether from X-rays, over-exposure to sunlight or atomic explosions. It is bad enough to have to suffer the development of spontaneous mutations in our non-dividing cells without adding to them the dangerous man-made hazards.

What has been said above indicates that geneticists are on the threshold of a historic breakthrough in their efforts to probe the secrets of heredity. There has been incredibly rapid progress in uncovering the structure and function of that most fundamental of substance DNA, whose molecules contain the blue prints governing the architecture of life. How is man going to face these problems of a genetic breakthrough? The gigantic problems posed by the mastery of nuclear energy which now and then threatens to destroy humanity will seem simple by comparison.

Ultimately we may be able to fashion living species to order, organisms with specific properties, just as we now produce machines or instruments. It is not too fantastic to imagine the time when the DNA may be manipulated to produce babies with predetermined traits and features! The moral, economic, and political implications of these possibilities are staggering. Is mankind ready for such powers? Just as we have not been prepared for the problems arising out of the mastery of nuclear energy, neither are we prepared for the ethical and other dilemmas with which genetics will confront us soon. It is time we begin to think about it.

L.H.N.

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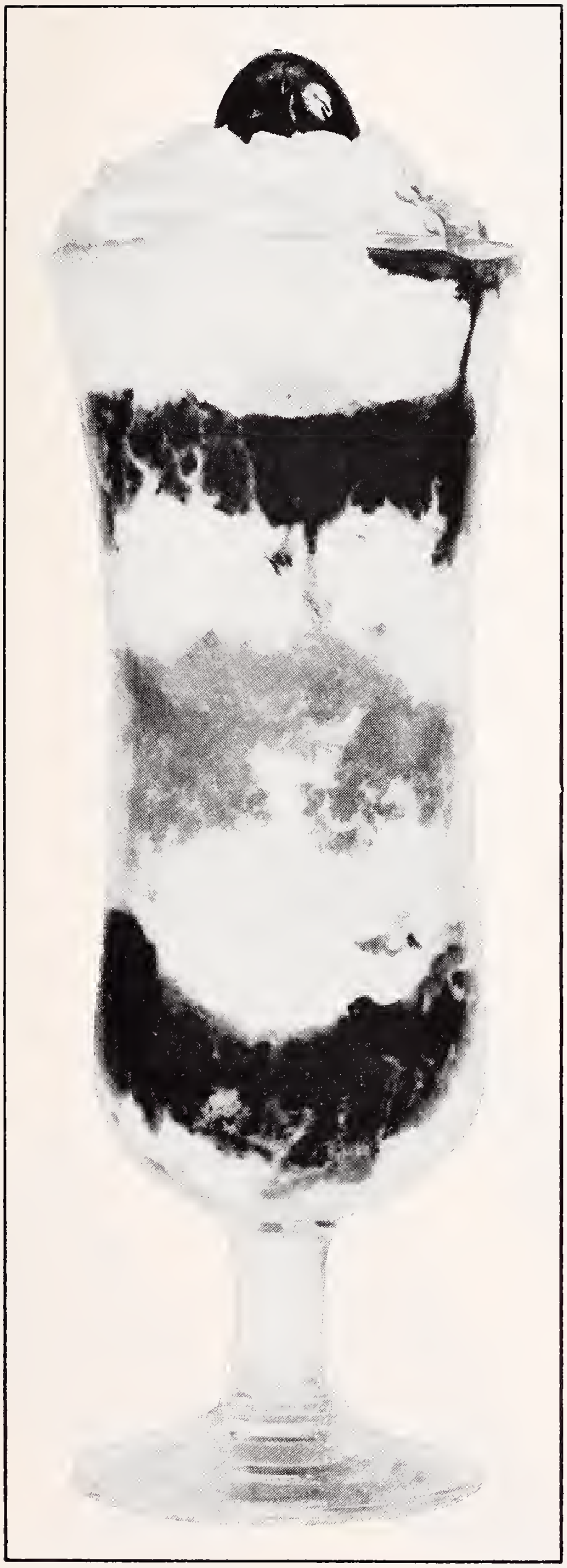

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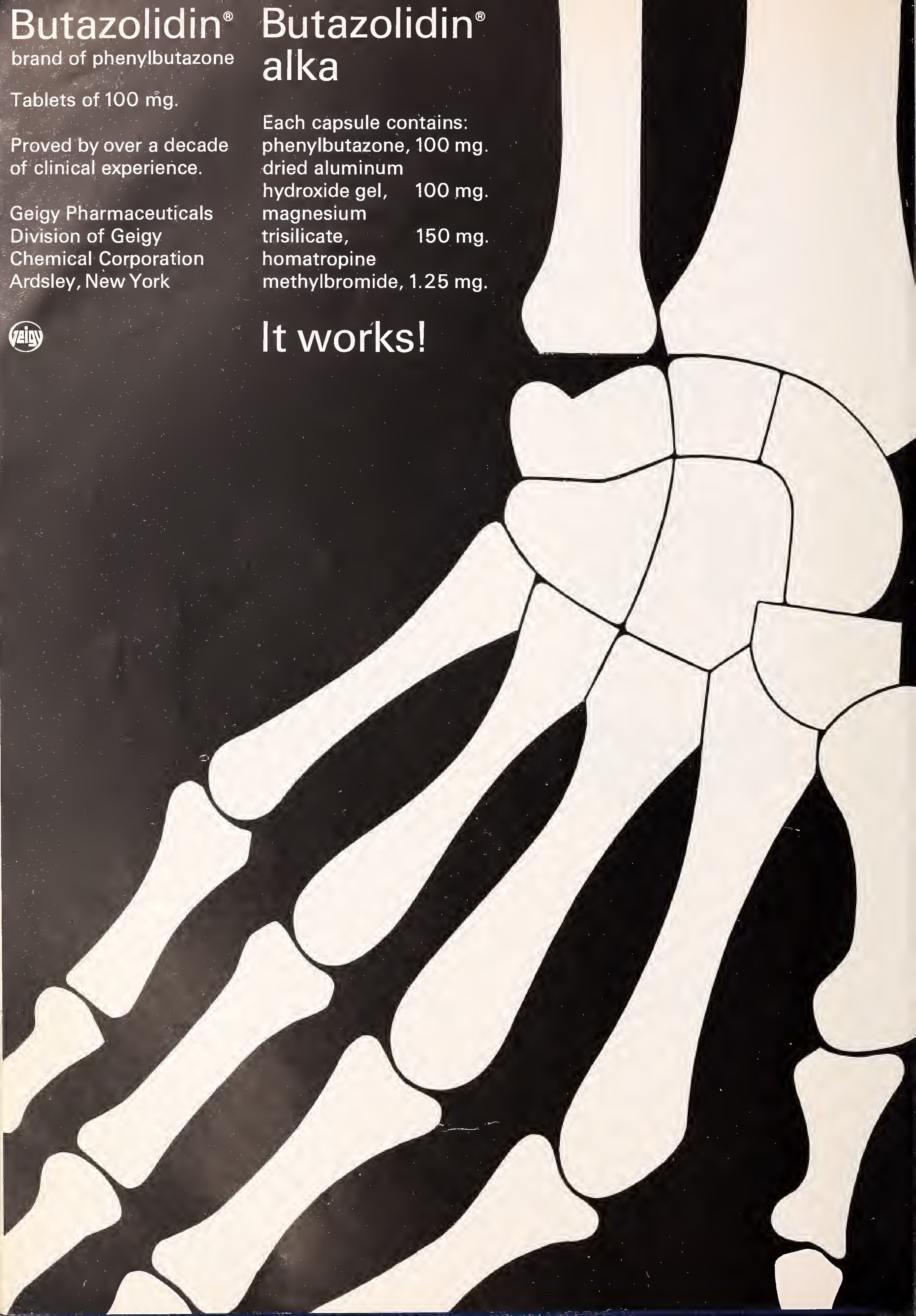

Dental Procedures Of Interest To The Physician

Physicians are frequently called upon to determine when it is permissive for a dentist to perform certain dental procedures on patients who are suffering from various cardiovascular diseases. The doctor is aware that hemorrhage may occur, that bacteremia can result from extraction of teeth. However, when and to what extent these may be expected is not always clear.

Bender and Seltzer[1] have made extensive studies of the incidence of hemorrhage, trauma and bacteremia after the various types of dental procedures and have clarified many hitherto unstated problems. They found that such procedures as filling teeth, fabrications of crowns, orthodontial procedures, and taking of impressions for dentures do not cause hemorrhage or bacteremia and should cause no concern. However, if the patient is on anti-hypertensive drugs and is subject to postural hypotension then he may develop an episode of hypotension and even syncope when he is changed too rapidly from a reclining position in the dental chair to an upright one. This can be more readily expected if there is considerable stress associated with dental procedures especially those of long duration such as mouth reconstruction or oral rehabilitation.

Whether local or general anesthesia should be employed in patients with heart disease has been under close study by Bender and his conclusion is very useful to the physician. He finds that if the patient is under a general anesthetic, the operator is more likely to use a more forceful manipulation and produce more trauma, than if the patient is being manipulated under a local anesthetic. Since hemorrhage and bacteremia are directly related to the degree of trauma, the authors advise against general anesthesia in patients suffering from cardiovascular disease. In principle any procedure that increases trauma, increases the threat of bacteremia.

The common problem of the dentist is exodontia or teeth extraction. If a tooth is firmly embedded and requires forceful rocking from side to side, the trauma is heavy and the procedure invariably produces a greater dispersion of bacteria into the blood stream, than the milder trauma encountered when teeth are quite loose, and the alveolar bone absorption is extreme. In the latter instance bacteremia is less likely than in the former. In the extraction of one or two firm teeth which have a great deal of alveolar bone surrounding them, there result a greater number of lacerated blood vessels and almost a 100 per cent incidence of bacteremia. In short there is a gradient relationship between trauma of extraction and the incidence of bacteremia; heavy trauma leading to a high incidence of bacteremia and mild trauma to a much lower incidence. An obvious corollary of this basic finding is that if one is interested in reducing the incidence of bacteremia, one should avoid multiple extractions at any one time.

Curtailment of the number of bacteria that enter the blood is the prime consideration in minimizing the incidence of subacute bacterial endocarditis in patients with rheumatic or congenital heart disease. This can be accomplished by use of a local anesthetic and limiting the number of teeth to be extracted at any one time in such patients. Bender and Seltzer have found this a more effective means of preventing endocarditis, than dependence on antibiotics alone; for it is only in mild cases of trauma, that antibiotic therapy is most effective.

The authors believe that hemorrhage after oral surgery procedures, is not a serious problem in patients that are receiving anticoagulant therapy, an experience that also corresponds with that of Behrman and Wright.[2] However, it is safer to operate when the prothrombin time is somewhat below the therapeutic range and when the procedures are tailored to reduce trauma to a minimum.

Periodontal procedures are performed to curtail and eliminate gingival inflammation and to prevent absorption of alveolar bone. Bender *et al*[3] have studied this problem also and have shown that the amount of trauma induced to eliminate gingival disease will determine the amount of hemorrhage and bacteremia. Deep scaling opens more blood vessels than superficial scaling does. Deep scaling is necessary when calcareous deposits have grown downward, pushed away the gum and inflamed it. This type of gingivitis is the result of the patients neglect to visit the dentist regularly. A physician can readily recognize this and refer his patient for periodontia, when superficial scaling will be sufficient. If gingival inflammation is also present, even slight trauma can produce bleeding, establish a portal of entry for the bacteria into the blood stream and threaten a valvular heart patient with bacterial endocarditis.

Bender and Seltzer[1] offer sound advice also in the management of a devitalized tooth. They point out the great advantages of root canal filling to preserve the tooth for this involves working inside the tooth, requires no anesthetic and induces no hemorrhage. This manipulative procedure is therefore the least likely to result in hemorrhage or bacteremia. In fact Bender found no bacteremia after conservative root canal procedures in which all instrumentation was confined within the root canal. However, as soon as the instruments were pushed beyond the canal into the surrounding bone marrow spaces, positive blood cultures were obtained in 31 per cent of cases.[3]

The treatment of an acute alveolar abscess or apical periodontitis can be a factor of great concern in the development of bacteremia due to the presence of more virulent microorganisms. Under such circumstances drainage should be established but preferably through the root canal rather than by ordinary surgical procedures.

The dental principles outlined by Bender and Seltzer are of practical importance to both the physician and dentist. They help clarify some of the problems a physician should understand when a patient with cardiovascular disease requires dental manipulation. They will lead to a more intelligent cooperation between physician and dentist, to the end of safeguarding the health of our patients.

L.H.N.

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Genetic Instability As A Source Of Aging

Senescense Is The Price Which Organisms Pay For The Luxury Of Differentiation.

—Raymond Pearl

Elsewhere in this issue is a review of Stroehler's book on "Time Cells And Aging." It is a scholarly overview of this difficult subject, and a statement of the unsolved problems, as well as of the lines of investigation which have been barely touched thus far. There are so many, that it is obvious they will not be answered in a few years. It might take as much as a score of years before we can begin to evaluate the feasibility of therapeutic measures directed towards slowing down this or that senescent process.

Comfort[1] defines aging as a biological process which causes increased susceptibility to disease or stresses. Thus cancer and atherosclerosis would then be considered biological phenomena which are separate from the phenomenon of aging. Accepting Comfort's view, a senescent tissue could be thought of as providing a favorable environment for some diseases such as cancer or infections, and at the same time one which withstands the stress of other diseases less well than younger tissues do.

Curtis[2] points out that the nature of the changes which occur in old tissues can be considered under three categories. One group of theories postulates accumulation of deleterious products of metabolism as a cause of aging. Certainly products such as collagen accumulate in some tissues, giving these organs the appearance of old organs. The skin is a familiar example. It should be noted, however, that deleterious products occur very markedly in some tissues and in others practically not at all. However, organs like skeletal muscle, which show marked aging changes, show little of any accumulation of unwanted products. In fact, changes in muscular ability are among the first sign of aging. Curtis rejects this theory of aging because it seems more likely that these products accumulate in certain organs as a result, not as a cause of the aging process.

The second set of theories are the so-called "wear and tear" theories. These postulate that each stress to which an organism is subjected takes its toll so that finally the organism wears out. Some patholögtists particularly have favored this view that senescence is the sum total of all the disease processes to which an organism has been subjected during his lifetime.

A third view is the mutation theory according to which the somatic cells of the body gradually accumulate deleterious genes by mutation which cause the cells and thus the organism to function less efficiently. This theory has the advantage of being a very definite concept, for if true, it could furnish a unifying view of the senescent process, and very satisfying as well, because it could furnish a rational basis for the ultimate control of the process. However, until now it had a disadvantage because it was very difficult to prove or disprove experimentally. With the discovery that radiation can accelerate the aging process in animals, a new avenue to the study of aging was opened. It allowed one to formulate the theory of aging on specific terms and to test it experimentally.

A few years ago, Curtis[2] designed a series of experiments to test the wear and tear theory. Mice were subjected to one of two generalized stresses. Nitrogen mustard and typhoid toxoid were administered in large doses so that half of the animals died. The survivors of chemical stress, however, had as good life expectancy as those of the controls. The experiment therefore failed to provide support for the view that stress, in one large dose is a factor in aging. How about stresses administered over a period of time? This experiment Cur-

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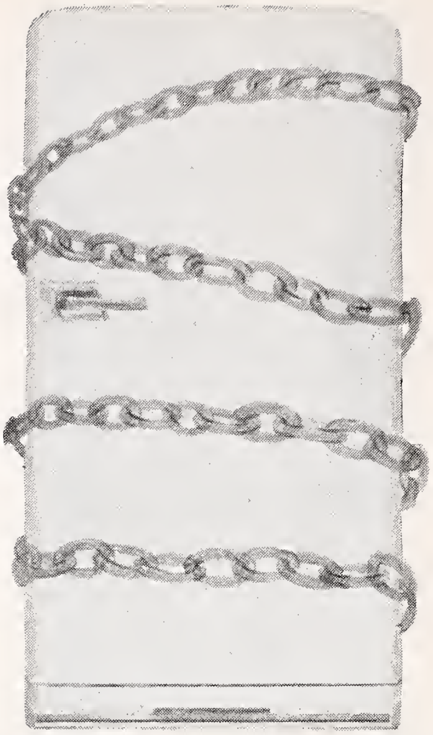

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tis also performed by giving poison three times a week for two-third's of the life expectancy of mice. After this severe treatment life expectancy of mice was unchanged. It is possible that a specific stress which severely damages a vital organ, such as mercury poisoning of the kidney could cause shortening of the life span by producing a "weak" link. But this shortens life because the normal aging process progresses to the point where the kidney finally fails. Here stress has not accelerated aging but it has shortened life.

There seem to be relatively few stresses from which the body cannot recover completely unless they have produced somatic mutations. Whether the mutations are experimentally produced, as for example by mutagenic agents like radiation, or whether they occur spontaneously, it is a virtual certainty that the cells and organs would be functioning less efficiently than they otherwise would, since most mutations are deleterious. The fact that radiation seems to accelerate the aging process and is also one of the most potent mutagenic agents known is very strong evidence in support of the theory. The problem in this theory was, that of developing a quantitative measure of mutations in somatic cells. Although this has not been accomplished directly, Curtis[2] has developed an indirect method for scoring the number of chromosome abnormalities in liver cells of mice and showing that this quantity is proportional to the mutation rate in these cells.

If a cell divides, most of the chromosome aberrations are obliterated by repeated cell divisions. There are a few cells in the body that very rarely divide spontaneously but can be made to divide if given a proper stimulus. The liver cell is a good example, for when a mouse is given 65 per cent of a lethal dose of C C14, then regeneration soon begins, and the accumulated mutations can be observed under the microscope. "Bridges" and fragments which do not take place in mitosis, appear and these aberrations increased steadily and reached a high value when mice were only twelve months old. By twelve months old most of the cells of the liver were carrying mutations. Radiation, the only known agent that accelerates aging also increases the number of mutations as measured by this method.

The results of Curtis' experiments indicate that somatic cells of mammals develop chromosome aberrations at fantastically high rates. Those strains of inbred mice which are long lived have fewer mutations than those of the short lived strain. These latter exhibit abnormal mutations in 90 per cent of all liver cells and presumably an equal proportion in all non-dividing cells, when the mice are hardly past middle age. If mutations occurred in the germ cell with anything like this frequency the species could hardly survive a generation. Either the gametic cells are somehow protected against mutations, or the process of meiosis preparatory to fertilization weeds out practically all defective cells. It is possible that part of the protection of germ cells against accumulating mutations is their constant cell divisions.

The cells in the body that are constantly dividing such as those in the bone marrow and intestinal mucosa are the longest lived and exhibit the least mutations. A mutagenic agent which affects only those cells, like nitrogen mustard, does not increase the aging process. Although nitrogen mustard breaks chromosomes in the bone marrow and intestinal cells, these are cells which undergo cell division quite rapidly, probably throw off the damaged cells in the process of a few cell divisions, and come out unharmed. Apparently, the organs containing cells which divide rapidly do not take part in the aging process. From this it would appear that only organs in which cells do not undergo cell division, or in which they rarely do so, take part in the process of senescence.

It has been known for many years, that in both mice and men, the offspring of relatively old mothers have more defects and a shorter life span than the offspring of young mothers. If the age of the father has any effect in this regard it is very small. On the basis of what has been said above, we might postulate that in the male, the spermatogonia undergo cell division continually and therefore, they do not build up mutations. On the other hand, in the female the oocytes stay in the ovary for a long time without undergoing cell division. Therefore, they can accumulate mutations as time goes on, some of which survive meiosis to endow the offspring with mutations. This concept to be sure is not proved, but it fits well with the present theory.

L.H.N.

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The Hormone Dependent Cancers

Some cells in the body depend upon hormones for their normal metabolism such as the prostatic epithelial cell and mammary epithelial cell. Such cells are termed hormone dependent. In castrate but otherwise normal males, the prostatic epithelial cell is small, has a low metabolic rate and does not secrete. When an appropriate steroid—testosterone, is administered, the cell enlarges, its metabolism increases and the cell secretes.[1] All of these processes regress when the testosterone is withheld, but the cell does not die in the absence of its supporting hormone, it merely shrivels. This cycle of growth and atrophy can be repeated scores of times in the same animal. Testosterone takes part in the oxidative phase of carbohydrate metabolism of the normal prostatic epithelial cell, but is not essential in maintaining its life.

Prostatic epithelial cells do become malignant. When they do, does the cancer cell retain the hormone responsiveness of its normal antecedent? The positive answer to this basic question resulted from beautifully conceived and executed experiments by Huggins for which he has just been honored by the Lasker Award. There was found one striking difference between the normal and cancer cell however. In the normal prostatic epithelial cell, testosterone participates in the growth cycle but in the hormones absence, the cell shrivels but does not die. The cancer cell however, is so dependent upon the hormone that in its absence the malignant cell does not survive. Huggins[2] reported that when testosterone was administered to previously untreated patients with prostatic cancer, the activity of the neoplasm was greatly accelerated, whereas when the natural source of testosterone was removed by orchiectomy, the cancer regressed and the malignant cells did not survive. Thus arose the concept of hormone-dependent cancers in which supporting hormones are of cardinal importance in maintaining the life of malignant cells and in the absence of these hormones the cancer cell dies.

It is now established that orchiectomy furnishes more effective control than do estrogenic compounds in inducing significant regession of cancer of the prostate in nearly every patient with this disease. The proof of this dramatic effect comes from studies of both the acid phosphatase and the alkaline phosphatase of the serum. Acid phosphatase rises with the dissemination of the cancer and alkaline phosphatase rises if the malignant cell invades bone.[1] The reduction of both acid phosphatase and alkaline phosphatase of serum are excellent indicators of the success of endocrine control of disseminated prostatic cancer.

The retention of hormone dependence by some cancer cells has been utilized for therapeutic purposes in other human neoplasms especially those of the thyroid endometrium and mammary gland. As long ago as 1896, Beatson[3] made a highly important discovery when he found that the removal of the ovaries caused regression of cancer of the breast in women. This was a classic observation the more noteworthy because it was done before the secretion of endocrine glands had been discovered. It was an empirical observation however, and the procedure declined when it was found that not all women with mammary cancer benefitted from oophorectomy. Because it was before the endocrine era, and the concept of hormone-dependence of cells had not been stated explicitly, it is not surprising that Beatson's work was not followed by either clinical or experimental studies of his highly useful treatment for disseminated cancer of the breast. They did not then know that after gonadectomy, the adrenals can support the growth of breast cancer in a considerable proportion of clinical patients in both male and female and that regression both profound and prolonged follows bilateral adrenalectomy.

The basic considerations which led Huggins to employ total adrenalectomy in mammary cancer, as well as gonadectomy was an observation by Woolley et al[4] that gonadectomy performed in young mice led to hyperfunctioning of the adrenal glands which permitted the development of the mammary glands and formation of mammary cancer. But of course, medical science had progressed so that by 1950 techniques for bilateral adrenalectomy and hormone replacement was easy to achieve because cortisone acetate was available. Thus adrenalectomized men and women are not incapacitated and are able to engage in all their usual activities. Furthermore, in well selected cases, they found that disseminated mammary cancer regresses profoundly and for long periods of time.[5] The recognition that the hypophysis controls secretion by the gonads and the adrenals, led Luft et al[6] to try hypophysectomy as a therapeutic procedure for mammary cancer, but it is not superior to removal of the gonads and adrenals in the control of disseminated breast cancer.

It is clear that procedures which have effectively modified the hormonal state, have yielded worthwhile benefit to many but not to all patients with disseminated mammary cancer. One of the problems that had to be overcome before final mastery of this type of cancer could be achieved, was to develop a model system for experimental attack on this problem. The first model system used was the mouse in whom the mammary tumor is usually hormone-independent. Huggins overcame this difficulty by finding a simple way of inducing mammary cancer in the rat which was hormone-dependent.[7] A single feeding of a special polycyclic aromatic hydrocarbon evoked tumors predominantly of

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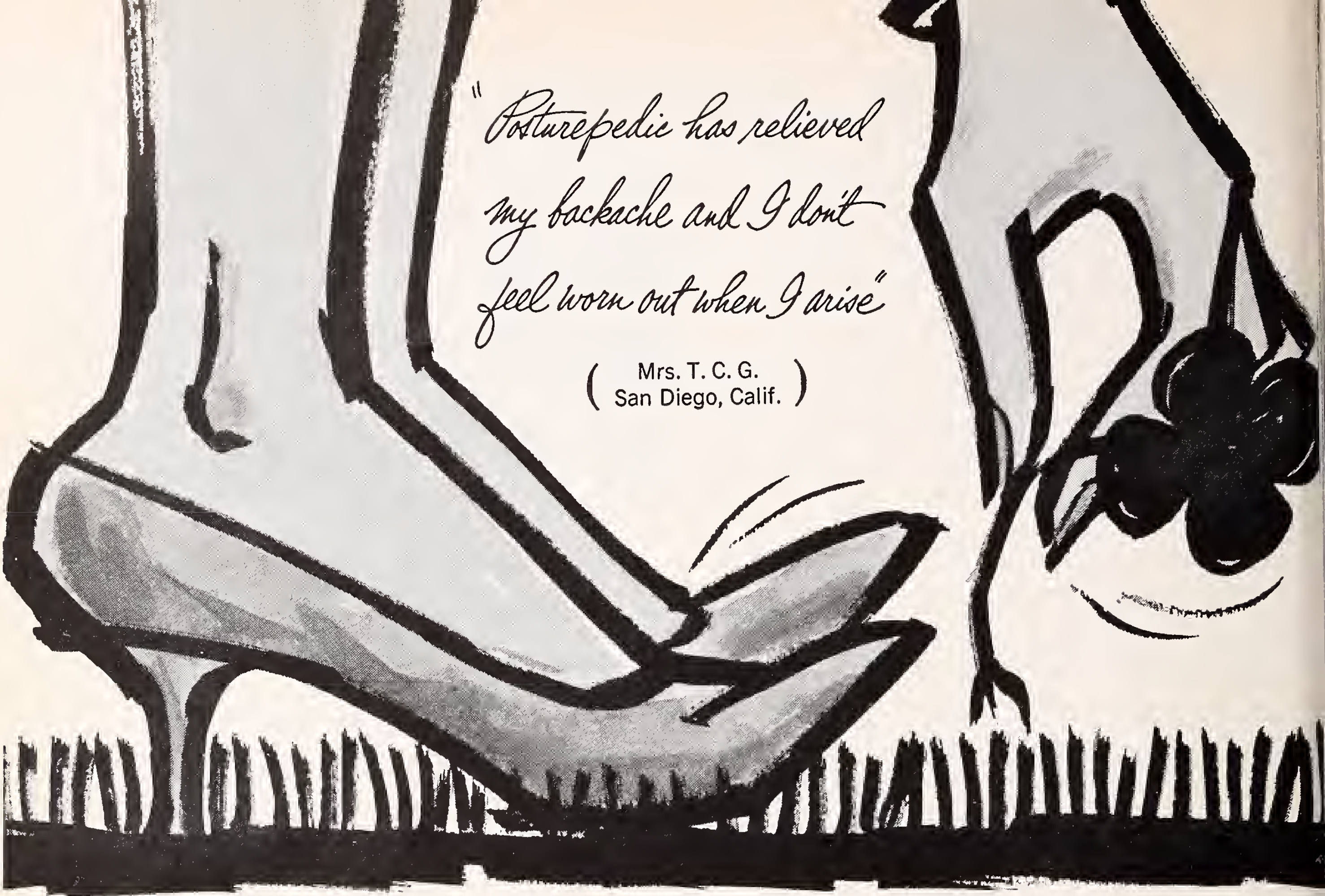
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the breast in the albino rat. The induction of mammary cancer is selective, invariable and rapid, the techniques are extremely simple. Under conditions which are easily satisfied every rat develops mammary cancer a truly spectacular phenomenon. Here we have a perfect model system because the mammary cancer induced is highly hormone responsive. Pregnancy always promotes their growth. Likewise, administration of progesterone accelerates the appearance of cancer, increases their number and augments the growth rates of the cancer induced by a single feeding of the hydrocarbon.

Huggins could cause regression of many of the induced mammary cancers by ovariectomy. Furthermore, he could also cause a large number of the cancers to be destroyed by administering large quantities of estradiol-17 β and progesterone. It seems as if estradiol-17 β in its biological action converted progesterone from an enhancer of breast cancer to a suppressor. Thus a new and beneficial approach has been found for those patients in relapse after adrenalectomy.

These encouraging results will undoubtedly lead to more extensive trials and use of other steroid combinations to control mammary cancer.

L.H.N.

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Science Tools 6. The Lethal Gene

A gene is now considered to be a molecule of a special deoxyribonucleic acid (DNA) which synthesizes a molecule of ribonucleic acid (RNA) which in turn synthesizes a special protein. All enzymes are such special proteins and are traceable back to a DNA in the chromosome. If for any reason a special gene is absent, then cellular abnormalities result, many of which are now known. Galactosemia is due to absence of an enzyme that splits galactose. McArdle's disease is an abnormality of skeletal muscle due to an absence of muscle phosphorylase. Gout is due to absence of an enzyme which is required for the kidney to excrete uric acid. Hemolytic anemia is due to a reduction in an enzyme in red cells glucose-6 phosphatase dehydrogenase. There are numerous other instances of gene absence or gene lethality and new ones are being discovered increasingly. Since atomic explosions increase mutations in living materials we may expect many more lethal genes in the future.

The term lethal is applied to those changes in the genetic make-up of an organism that produce effects severe enough to cause death. We know now of alterations in the number of chromosomes, of changes in chromosome structure and of gene mutations. Not all gene mutations are necessarily lethal. If an organism loses ability to synthesize an amino acid, and if the organism is grown in an environment without this amino acid then the mutation would be lethal. However, if it is grown in an environment in which the amino acid is supplied the same mutant becomes viable. If a higher organism, became unable to synthesize glycine, this amino acid would have to be supplied from an external source to prevent a lethal outcome as we do to a growing chick. It has been suggested that a mutation which occurred in the course of evolution is responsible for the human requirement of ascorbic acid (Vitamin C) from the outside.

Some animals appear to be able to synthesize ascorbic acid, but primates and guinea pigs cannot and, unless it is provided in the diet, lethality results. It is therefore possible to distinguish a lethal gene by effects which are not compatible with life, unless compensated for in some other way. How lethal genes originate is speculative but they may originate in spontaneous mutations or they may be produced by mutagenic agents such as chemicals or x-irradiation or atomic explosions. The frequency of spontaneous lethal recessive mutations have been measured in drosophila where they have been found to be between 32 per cent of chromosome 3 and 41 per cent of chromosome 2. In man they cannot easily be determined but one such estimate is that normal heterozygous persons carry an average of eight recessive lethal or sublethal genes.

Lethal genes can be used as tools for analyzing the development and differentiation of mammalian embryos and for studying the genetic control of these processes. Lethal genes have been shown to produce a wide variety of morphological, physiological, biochemical and metabolic abnormalities, which may lead to death of the organism before or after birth or even as late as maturity. Of course, ultimately lethal gene action resides in an error at the molecular level, but its expression may occur at any of the various levels, the level of the cell, the tissue, the organ or the organism. Gluecksohn-Waelsch[1] points out that frequently the lethal effect is the end result of a long chain of processes that are started off by one primary gene controlled abnormality. Occasionally a lethal gene results in the suppression of normal development of a vital organ and in this way causes death of the organism. The author has described animals homozygous for a gene Sd in the mouse which are born completely tailless and die soon after birth because of an almost total lack of kidneys. The steps by which such a lethal gene leads to the absence of kidneys has contributed to the causal analysis of normal kidney development in the mammal.

Recently a new mutation in the mouse called "lumbarless" was discovered. It causes death of certain homozygotes in early adulthood as the result of paralysis of the posterior part of the trunk. Lumbar vertebra may be missing or be so abnormal that they appear jumbled and the spinal cord is severely abnormal. Here was a chance for studying the relation between neural tube and cartilage forming material. What was found was a nucleotide material in the spinal cord which seemed to be responsible for promoting such cartilage formation. Here then is an excellent tool for studying the interaction between spinal cord and somites in the embryo.

Another such lethal gene results in phocomelia which in the homozygous condition causes death of the newborn within a few hours after birth as a result of cleft palate. Phocomelia newborn mice show severe shortening of the extremities and other skeletal abnormalities which remind us of those described in human babies of mothers who had taken thalidomide.

It is possible to produce congenital malformations by injecting insulin in a chick embryo or by thalidomide in a human that closely simulates the effect of a lethal mutation. Clearly such congenital abnormalities as well as lethal mutations can lead towards the identification of the causality of the defect. But it can do more. Because of their effects on development and differentiation, lethal genes offer particular promise as tools in the investigation of cell differentiation and cell genetics. The problem of cell differentiation during embryogenesis is still far from solved. Lethal genes may well turn out to be the tool of tools providing experimental material in which abnormal cell differentiation occurs. Although the problem of cell differentiation is far from solved, we at last have a tool, the lethal gene which provides experimental material to reveal, through abnormal cell differentiation, the factors operating in the phenomena of normal interaction and regulation during embryogenesis.

L.H.N.

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Coincidence vs. Evidence In Drug Evaluation

Just what these new (FDA) regulations will do to the introduction of new remedies will not be apparent for some time. A reasonable guess is that fewer new drugs will be introduced and the prices of drugs will be higher because of the new costs added to the testing. The difficulty of separating coincidence from evidence is seldom appreciated. Common symptoms such as thrombophlebitis, skin reactions and headaches may be coincidental with the administration of various remedies. Intensive investigations may be necessary to separate the coincidence from the incidence. — Morris Fishbein, M.D., in *Postgraduate Medicine,* June 1963.

Doubt And Disbelief In Clinical Progress

Not infrequently, it takes years and sometimes decades of widespread clinical experience to evaluate the relative merit of a drug in given conditions. From such long experience, a medical consensus generally emerges but even then some qualified physicians refuse to go along with their colleagues. History teaches that authoritarian bodies often have been guardians of orthodoxy rather than champions of progress. Medical experts rejected Jenner's smallpox vaccine, Pasteur's anthrax vaccine, Lister's theory of antisepsis and Semmelweis' discovery of the cause of childbed fever. Cod liver oil was rejected as worthless by the Council on Pharmacy and Chemistry of the American Medical Association. When Prontosil, the first sulfa drug, was introduced in the United States, it was greeted as another quack remedy by an outstanding American authority on infectious diseases. In the early 1930's, the same authority dismissed early English reports on penicillin as incredible and refused to employ for clinical testing a culture of penicillium that had been brought to him by one of his associates. He poured it down the sink.—Theodore G. Klumpp, M.D., at Conference of Professional and Scientific Societies, Chicago, Ill., June 28, 1963.

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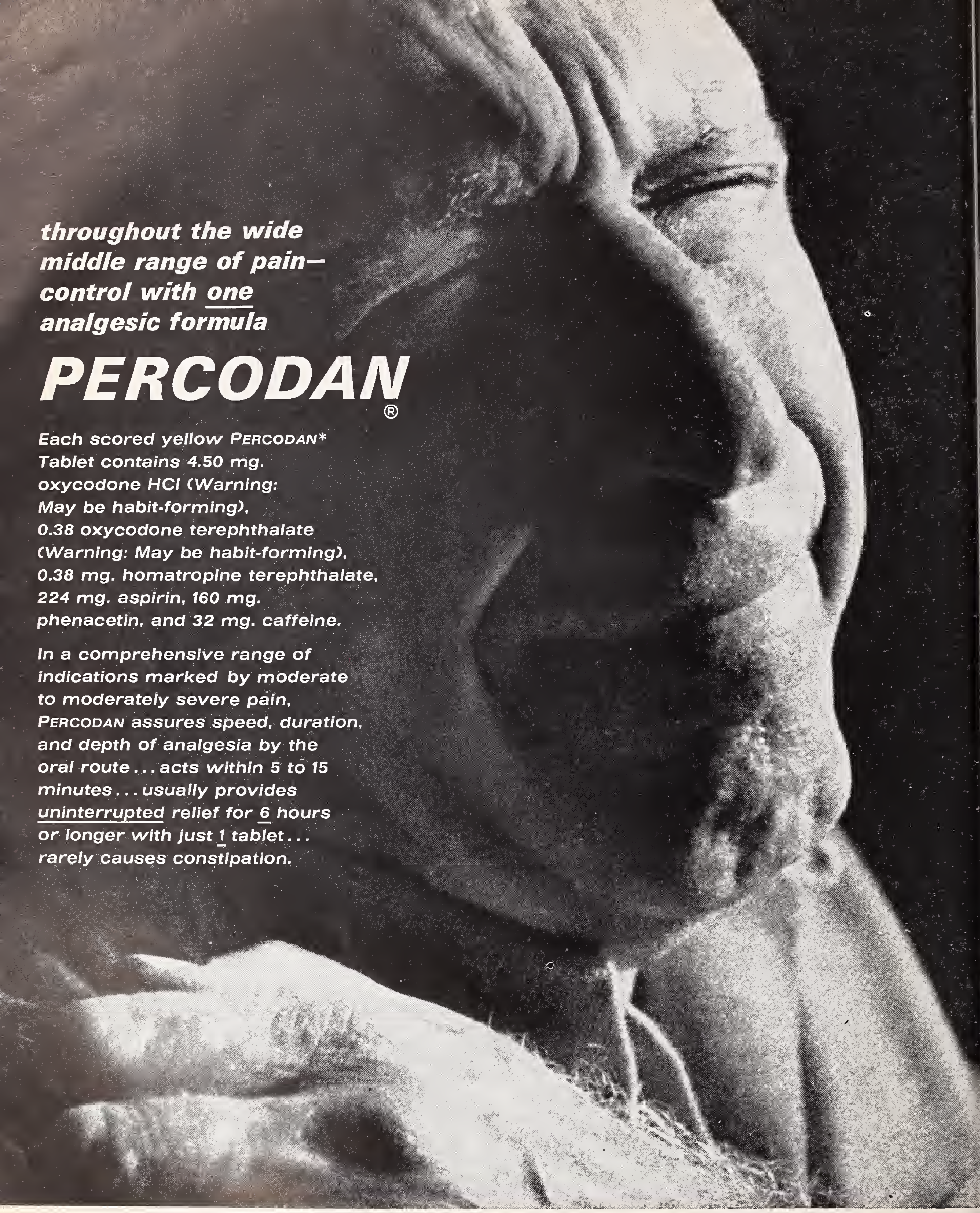

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I. The Clinical Story Of Radiation Damage

Marshall Brucer, M.D.

■ There are thousands of things for a physician to worry about: From Enovide in Thrombo-enbolics to increased lung cancer in English emigrants to New Zealand (not tobacco). Nuclear accidents (I include war as a political accident) may be one of the minor subjects: Since no physician can know everything about everything, it is probably a proper detail only for a few narrow specialists. However, every physician must be *aware* of the medical problem and the state (or nonexistence) of therapy.

In the spring of 1963, a well-known theoretical physicist gave a scholarly lecture on the implications of nuclear war. He was questioned by an equally well-known mathematician who asked about medical therapy. The answer was the familiar fund-granting whitewash usually reserved for Congress: *"We are working tooth and nail on chemical protection"* (which we aren't); *"We are probing for the radiobiological cause for damage"* (a sterile procedure since 1904); *"We are pouring money into the genetics of radiation damage"* (for the fruit fly this is good). It seemed almost implicit that the proper method for doing medical research was to set up a disease as a public image and then throw money at it.

In 1870 there were no automobile accidents because there were no automobiles. In 1940 there were few nuclear accidents because there were few nuclear plants. This is now changing. Radiation installations from the smallest diagnostic X-ray machines to the largest nuclear reactors are encompassing the globe. Nuclear accidents have changed from potentialities in the 1940's to possibilities in the 1950's, to probabilities in the 1960's. Murphy's sixth law still stands: If an accident can occur—it will.

HOW TO LOOK AT RADIATION DAMAGE IN THE HUMAN?

There are lots of ways of approaching the problem.

Therapeutic radiation is given purposely. It is hoped that the radiation will cause damage, but the damage is carefully assessed beforehand; it is controlled. Therefore, this is a topic of proper concern for radiotherapists. It is not damage in the sense that it is unnecessary and unwanted.

Diagnostic radiation did cause some damage early in the century. Some patients might still be and always will be hurt with diagnostic radiation, either because of lack of skill or lack of care or out-and-out quackery. But, for the most part, people are not hurt with diagnostic radiation.

Radiobiological radiation can be applied at any level and to any plant, animal, or chemical. Usually, it is done with a purpose. Like therapy, it is controlled. It is a necessary and desirable damage.

Accidental radiation is a different matter. It is always undesirable, but no matter how often we say accidents are unnecessary, they still occur. We may legislate against them, but they still occur. The atomic energy industry in the United States is the safest (after the corset industry) place to work in the United States. The chances for a serious nuclear accident are much less than the chances of drawing a perfect bridge hand. About twelve impossible things had to occur in exactly the right order to achieve the 1958 Oak Ridge nuclear accident. The chances of this occurrence were so small that it just couldn't possibly have happened;—but it did.

Noncontaminating Radiation

We could consider all accidents as either contaminating or not contaminating the patient. The presence or absence of contamination not only will change methods used in diagnosis, but also may change the approach to therapy.

The X-ray machine is a common example of a source of noncontaminating radiation. Electromagnetic radiation (X-rays) of around 100 kev are propagated through space and meet the body. Some place within the body, a photon in the beam of electromagnetic rays might come close enough to or be captured by one of the atoms in the body, or it might go completely through the body without any interaction; or it might interact on the surface of the body, or just before it reaches the surface. Within the atom of interaction, the low-energy photon disappears and a negatively charged electron is pushed out of place. The atom of interaction has lost a charge and so it is now an ionized atom. The electron is "bigger" in an electromagnetic sense, and so its likelihood of meeting up with other atoms is much greater. It does not penetrate very far into the body and it causes an ionization along its track losing some of its energy each time it produces a third generation. Each of the third generation electrons might produce a fourth and fifth, etc. generation until the energy is below that necessary to remove another electron from its atom, then it only moves the electron within the atom, but does not remove it—this is called excitation.

With each interaction, some of the energy is dissipated as heat; thus, three things occur: (1) ionization; (2) at a lower energy, excitation; and (3) at a still lower energy, heat production. Each time an electron is removed from the atom, and usually it is from the shell close to the nucleus, an electron from the next higher shell jumps in to take its place, and then an electron from the next higher shell jumps in to take its place, etc. until the positively charged portion of the atom captures one of the many free electrons not already committed to an atom. Each of these jumps results in more radiation. All this happens very rapidly. In a very small fraction of a second, an electromagnetic photon has disturbed the positions of many electrons in many atoms. For any one single event about half the energy has been in ionization; the other half has been excitation. Over the entire path of any one photon there have been relatively few ionizations, but an enormous number of excitations.

During a very brief period of excitation, the atom is chemically highly reactive, much more so than in ordinary chemistry. This chemical reactivity is probably what causes the ultimate biological effect, but it is extremely short-lived. This is a noncontaminating form of radiation.

Contaminating Radiation

The best known example of a contaminating radiation (to a newspaperman) is the Sr^{90} atom formed in a bomb explosion. The Sr^{90} is carried to the upper atmosphere. It usually agglomerates to form an oxide or a carbonate and becomes a multi-molecular particle. This is now a clump of material of appreciable but small size. It may be washed down to the earth in a rain storm or just fall with gravity and finally be breathed into the lungs of a human being. Within about a fifth of a century, half of these Sr^{90} atoms will disintegrate; the disintegration gives off a half-million-volt electron. This is the same kind of electron that is called a secondary in the electromagnetic interaction, but it is of much higher energy, and this electron goes through exactly the same process that was achieved with the secondary electron. But the original Sr^{90} atom has lost a charge, and therefore it is no longer strontium; it is now yttrium. About half the Y^{90} atoms will disintegrate within a period of two and a half days, and then they too give off an electron to become Zr^{90}; the same kind of electron only it has a very high energy of about 2¼ Mev. The chain of electron production causes the same kind of ionization and excitation and secondary and tertiary photons, each losing a little energy in each event until all of the energy has dissipated. It is the same thing that occurred with electromagnetic radiation with one great exception: it might not occur immediately; it might occur a long time after the molecule has been absorbed by the body.

While the atom exists as a strontium or yttrium or zirconium atom, it follows the normal metabolism of strontium, yttrium or zirconium atoms. Since we never talk of one atom, but of thousands upon thousands of atoms for even the smallest dose, the result is a continual but decreasing radioactivity. In noncontaminating radiation the event occurs instantaneously (microseconds). With contamination it also occurs instantaneously, but the occurrence may not be until many, many years after the isotope has been formed.

A DISTINCTION BASED UPON THE PART OF THE BODY AFFECTED

We could also classify radiation by the part of the body affected. It is really based upon the part of the "thing" affected, because the same things can happen to a Geiger tube that happens to a human body. Or, for that matter, by stretching the definition, the same thing can happen to a piece of metal that happens to any organism. We can classify radiation damage as being *somatic* or *genetic*.

Somatic damage is the kind that affects the body, cell, or material within the lifetime of the particular thing being irradiated.

Genetic damage is the kind that produces an effect in the reproductive mechanism, not necessarily in the original nongenetic part. It is then transferred to the next generation.

Usually, the differentiation between somatic and genetic radiation is confined to living organisms that do have a genetic type of reproduction. It can be applied to inanimate objects, but only by considerable distortion of the original meaning. For example, a piece of steel that has been contaminated with Co^{60} may or may not affect the original piece of steel. This could be considered a somatic effect. The piece of steel then becomes a piece of scrap iron that is put into the furnace to make other pieces of steel and the contamination is transferred to the next "generation" of steel. This would be a kind of genetic transfer. But, the words are not usually so applied.

We could also make a distinction between radiation effects that occur locally and at a distance. For example, one of the first items noticed in radiotherapy was that when a radiotherapist irradiated one metastasis a distant metastasis got smaller. The part of the body being irradiated is not necessarily the part affected. One of the great stimuli to the chemical theories of radiation damage has been the necessity for explaining distant effects.

Another distinction that has been made has been to distinguish *immediate* from *delayed* effects. This is the same kind of thing as the somatic and genetic or the local and distant effects, but it is a different parameter of observation.

THE DISTINCTION BETWEEN ACUTE AND CHRONIC

Still another method of distinguishing between types of radiation damage has been to call some things *acute* and others *chronic*. The words are not usually precisely defined. *Acute* can mean microseconds or it might mean small fractions of a lifespan. But, *chronic* can also mean small or large fractions of a lifespan. Also, when we talk of something as the *acute radiation syndrome* it is necessary to make a distinction between the *acute radiation acute syndrome,* the *acute radiation chronic syndrome,* the *chronic radiation acute syndrome,* or the *chronic radiation chronic syndrome.* One of the reasons for the confusion that exists in radiobiological thinking is the fact that the words acute and chronic mean different things to different people. Some may talk about *acute* radiation deaths that means a lethality within thirty days; others may be talking about lethality occurring within sixty days; others may be talking about lethality that occurs before some definition of a "normal" lifespan. The various classifications of radiation damage may be mixed. Two persons will talk about the somatic effects from an acute radiation genetically transferred or the chronic effects in the third generation, and the two authors really mean the same thing. Any kind of distinction can be made so long as it is understood.

DISTINCTIONS BASED UPON EFFECTS OF RADIATION

A distinction between various kinds of radiation can be made purely on the basis of the effect. We may talk about purely physical effects; the temperature is increased, the weight is decreased, some materials are vaporized and so change their state from solid to gas, or, some may be liquified, or, some change from a liquid to a colloid.

Or we may make distinctions based upon purely chemical effects. A sufficient amount of radiation can make obvious changes in the chemistry of the material. Certain highly specific kinds of chemicals (such as enzymes) may be changed by radiation. Some radiation produces a change in the elemental composition of a material. For a long time it was thought that radiation did nothing more than break down long-chain into short-chain compounds. Early in the history of radiation and now again it appears that there is also a polymerization. How this may or may not affect a substance made up of many atoms depends to a large extent upon the number of atoms involved.

We might make a distinction based purely on ecology or economics. The irradiation of the male Screw Worm may increase the production of beef, which causes an over supply in the market, which causes an economic change in the price of meat. Economic changes inevitably lead to political changes, so there can be political effects of radiation.

Finally, we could make distinctions purely on clinical grounds. The irradiation of a healthy person might be less likely to cause sickness than the irradiation of a sick person. The irradiation of a baby is different from the irradiation of its mother; or when both are in one body, there might be differences in the effects.

NONE OF THESE DISTINCTIONS ARE ADEQUATE

All these distinctions are neccessary in thinking about radiation damage, none is adequate in itself. For example, the irradiation of a body with very high-energy electromagnetic radiation might result in a transmutation of the atom from a nonradioactive to a radioactive material. Usually this is in such a small quantity that it is unnoticeable, because such events are highly improbable. However, the irradiation of the body with neutrons is both noncontaminating and contaminating. The neutron itself causes a terrific amount of ionization, but it also might result in transmutation from a nonradioactive to a radioactive form. People who have been irradiated with slow neutrons become perceptively radioactive themselves. The same thing is true with almost any kind of radiation to a greater or lesser extent. The distinction between contaminating and noncontaminating is satisfactory only within fairly wide extremes.

Almost every simple distinction (somatic-genetic or acute-chronic or sick-healthy or live-dead) is inadequate. First of all, we have to make a definition of radiation, and where it comes from; then we have to describe one kind of effect, the acute radiation syndrome, for we do know something about the subject. We don't have to talk about basic radiation physics, because this is fairly well known and is repeated in many textbooks. But, there are two subjects that have had little attention or are going through tremendous changes. One is on the biochemistry of radiation, the other is long-term effects.

A third subject should then be considered: the diagnosis and treatment of radiation damage. We should also try to summarize for physicians who are not experts in the radiation diseases just what can and cannot be done in the same way that many other diseases are summarized. This will be inadequate and it is undoubtedly going to be changed. The change, however, does not occur as rapidly as the newspapers would have us believe.

After this segment there is the necessity for talking about questions of radiation protection; this is fairly well known. However, this subject has been a political football during the 1950's and it should be summarized again. Since we are going to talk about accidents, we have to talk about how many people are involved.

In addition to what we in the United States may feel about radiation there is a necessity for looking at what other people think about it. A segment of foreign comments will follow; some not by physicians. Often the impression of a nonphysician who happens to be expert in some nonclinical phase of radiation is far more important than the impressions of a clinician who is not an expert.

Finally, there is a necessity for a bibliography. A simple listing of titles is not sufficient. One book that was written on the effect of radiation in humans about ten years ago has absolutely nothing to do with radiation in humans.

Any physician who attempts to treat diabetes without years of training, much in fields outside of diabetes, is probably going to fail; the treatment is not simple. The same thing can be said of almost every disease. The medical aspects of radiation damage are not simple now and they never will be. Therefore, it is impossible to write a simplified (how to do it) manual on the treatment of radiation damage. The subject may not be so statistically important as the treatment of heart disease, but a physician is supposed to be able to treat every patient, not just a statistical preponderance of most likely diseases.

"The Methodology Of Science"

When a man is talking about scientific subjects, the little word "I" should play no part in his expositions. But when he is talking about the purposes and aims of science, he should be permitted to speak of himself; for a man experiences no aims and desires so immediately as his own. The special aim which I have constantly kept before me is logical unification in the field of physics. To start with, it disturbed me that electro-dynamics should pick out one state of motion in preference to others, without any experimental justification for this preferential treatment. Thus arose the special theory of relativity, which, moreover, welded together into comprehensible unities the electrical and magnetic fields, as well as mass and energy, or momentum and energy, as the case may be. Then out of the endeavor to understand inertia and gravitation as having a unified character there arose the general theory of relativity, which also avoided those implicit axioms which underlie our thinking when we use special co-ordinate systems in the process of formulating basic laws.—Albert Einstein. *Essays in Science.* New York, Philosophical Library, Inc., 1934, p. 113.

II. Definition Of The Radiation Complex

A. The Characterization Of Radiation*

Marshall Brucer, M.D.

■ The word "definition" is too demanding to use. It has mathematical overtones of the word "definite". The word "radiation" is too ubiquitous to use. It is hard to imagine energy that does not radiate in some way or other. Of course, we mean ionizing radiation: the kind that removes an electron forcibly and suddenly from its current atom of residence, even if the ion exists as an ion only momentarily.

This ionization is not what causes the major biological effect. "Excitation"—just enough energy to move, but not to remove the electron—is probably the main cause. But historically we measure electrical changes (because it is easier, not better). The word as used here means alpha rays and beta rays and gamma rays and X-rays, but not ultraviolet rays, or visible light, or heat, or electricity.

The old concept of "ionizing radiation" is good enough provided we use the words for understanding and not for courtroom legalistics. But even a limited description has too many exceptions to be a definition. Man has been radioactive for a long time. The biosphere presumably has been radioactive for even longer. We cannot imagine a non-radioactive environment. Once we have answered every question in science (along with defining life) we shall be able to define radiation.

But There Are Differences!

A human body contains from 200 to 300 billion billion atoms of radioactive potassium—about 0.1 microcurie. This is different (and about two orders of magnitude greater) than distant fallout. The astronaut will be exposed to high-energy cosmic rays; this is different than the exposure of a person living in southwest India. The Denver resident and the Boston resident are both exposed to cosmic rays, and to the radioactivity of the earth but in different amounts; these are different patterns. If each person were exposed to an atom bomb explosion, this would be a still different pattern. Each might have hyperthyroidism and be treated with radioactive iodine, a still different kind of exposure. Even though we may not be able to define radiation precisely, we can still characterize it in such a way that we may distinguish one kind of exposure from another.

12 And Only 12 (In This Article) Things To Consider

1.) DOSE IN RADS

Each person is exposed each day to a fraction of a millirad just by being alive. The exposure comes from his own K^{40}; is neccessary, unavoidable, and may be desirable. "Big" is different from "small" and this is probably the first major item that goes into a characterization of radiation exposure, but it is hard to say what "BIG" and "SMALL" mean. One ionizing event may sterilize the egg of the small animal. This may be undersirable (at least to the parents of that particular egg). Some small animals can live through thousands of r of exposure with, apparently, no ill effects. We can't say big or small unless we relate the words to the thing that is of interest. A thousand rads is "BIG" to humans; it is "SMALL" to a weevil.

We must establish some sort of mean dose and then an overwhelming and an insignificant dose. This measure should extend over the range of interest to a particular animal. The LD_{50} dose for the 30 days following acute radiation exposure is a good enough mean. It doesn't matter whether it is correct or not; neither does the standard deviation have to follow the true meaning of a "standard deviation;" we can use a first approximation; the definition can be changed to fit a known or assumed distribution.

There are six classes; the central classes each contain a third of the population, the two outer classes less than one sixth each, and the extremes are unusual. For example, in man we can assume that the ${}_{30}LD_{50}$ dose for acute exposure is 750 rads. The standard deviation is 250 rads. This means that 0 to 250 rads is the third standard deviation below the mean. It would be unusual (medically, not politically) to include these in a population of acute radiation accidents. There is no such thing as "0 rad" of radiation or a lowest "standard deviation," but so long as we know that this is really an oversimplification, it can be used for talking about the whole picture.

Two hundred and fifty to 500 rads is the second "standard deviation" below the mean. It is improbable that it would be lethal. Five hundred to 750 rads is one standard deviation below the "assumed" mean. Seven hundred and fifty to 1000 rads is one standard deviation over. Between 1250 and 1500 rads almost every person will die, but not necessarily 100 per cent. To simplify (or rather oversimplify) for the purpose of looking at the whole picture, we are going to say that 100 per cent of persons will die from an acute radiation dose over 1500 rads. This is not the true definition of a third standard deviation over the mean, and it certainly is not a true picture of acute exposure. At least one person has lived with a dose of more than 1500 rads, but this is a simplification that is necessary because other factors must be taken into account simultaneously.

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* *Presented at the City of Hope Symposium on* Supervoltage Irradiation and Genetics, *Duarte, California, June 1, 1963.*

2.) THE RATE OF EXPOSURE

A man cannot eat 15 tons of food in one day, but he probably will eat 15 tons in his lifetime. Similarly, it is almost obvious that an exposure to radiation over an extremely short time has a different biological effect from the same dose delivered over a very long time. The dose absorbed is by definition a rad. But the exposure is usually measured in roentgens. It is easier to think of the essential difference (and a constant reminder of it) to speak of the dose in rads and the rate in roentgens.

There is no such thing as an "average rate of exposure" but, for convenience, we will accept 1 mr/sec. as the average rate. A simulated standard deviation is a factor of 10 from this. Thus, a slow radiation exposure is less than 1 micror/sec.; a fast exposure is greater than 1 r/sec. Table I shows the magnitude of total accumulated dose with one set of dose rate divisions applicable to human exposures. Other objects would need other scales.

The probably true distribution of the rate of exposure for the entire population is that 100 per cent of the population receives many very short high-rate exposures (cosmic rays), but 100 per cent of the population also receives a continuous low-rate exposure (K^{40}).

3.) THE ENERGY OF IRRADIATION

A proper energy scale does not distinguish between a 4 Mev alpha particle and a 4 Mev gamma ray. One may never get through the skin; the other may go completely through the body without interaction. Since we are interested primarily in the effect of the radiation, we should be talking in terms of penetration. But we can't use the simple tenth-value layer concept because various kinds of radiation approach the body (incidentally, not a sphere) in different ways. A tenth-value layer from the inside of a bronchus is different from the tenth-value layer from the surface of the heel. In this particular (practical but nonphysical) meaning of the word energy, we mean tenth-value layer. But we also mean pharmacologic position. We also mean kind of radiation. We also mean depth of effect, position of effect, approach to the body, type of material. For the purpose of talking about this biological-physical mutant definition, we shall assume that, in general, there is less biologic effect on the total organism from the extremes. Most of the common biological effects are from X-rays and gamma rays. Whether this is right or wrong, it establishes a scale. It is probably true that most of the biological effects from radiations that we are naturally heir to are from the high-energy alpha or low-energy beta particles or from the continuous bombardment by very high-energy electromagnetic rays. We assume an importance for X and gamma rays that is probably not true.

TABLE I

TOTAL DOSE (r) BY DOSE RATE DIVISIONS
(ARBITRARY; FOR HUMAN EXPOSURES)

	SLOW			AVERAGE			FAST
	Dose Rate per Second in r						
TOTAL EXPOSURE (r) IN ONE:	0.00000 1r (1 μr)	0.00001 (10 μr)	0.0001 (100 μr)	0.001 (1 mr)	0.01 (10 mr)	0.1 (100 mr)	1.0 (1 r)
Second	1.0 x 10^{-6}	1.0 x 10^{-5}	1.0 x 10^{-4}	1.0 x 10^{-3}	1.0 x 10^{-2}	0.10	1.00
Minute	6.0 x 10^{-5}	6.0 x 10^{-4}	6.0 x 10^{-3}	6.0 x 10^{-2}	0.60	6.00	6.0 x 10^{1}
Hour	3.6 x 10^{-3}	3.6 x 10^{-2}	0.36	3.60	3.6 x 10^{1}	3.6 x 10^{2}	3.6 x 10^{3}
Day	8.6 x 10^{-2}	0.86	8.64	8.6 x 10^{1}	8.6 x 10^{2}	8.6 x 10^{3}	8.6 x 10^{4}
Month	2.59	2.6 x 10^{1}	2.6 x 10^{2}	2.6 x 10^{3}	2.6 x 10^{4}	2.6 x 10^{5}	2.6 x 10^{6}
Year	3.2 x 10^{1}	3.2 x 10^{2}	3.2 x 10^{3}	3.2 x 10^{4}	3.2 x 10^{5}	3.2 x 10^{6}	3.2 x 10^{7}
Life	2.3 x 10^{3}	2.3 x 10^{4}	2.3 x 10^{5}	2.3 x 10^{6}	2.3 x 10^{7}	2.3 x 10^{8}	2.3 x 10^{9}
Approximate Range in Dose	>Maximum Permissible Dose						<Therapy Dose

4.) NUMBER OF EXPOSURES, 5.) DURATION, and 6.) INTERVAL

If we accept each cosmic ray as a separate exposure, then each person during his lifetime receives many millions of exposures. The K^{40} radiation already inherent in the body does not give off continuous radiation, but there are so many atoms (4000 disintegrating each second) that we can consider the combined action of all the atoms as one continuous exposure. This means that everybody gets one continuous exposure and everybody gets millions of separate exposures. A person who gets a therapeutic course of X-rays gets an additional 20 to 40 exposures. A person who does radiochemical preparations for a living may get additional thousands of exposures during his lifetime. As a working approximation, the average is a thousand exposures and the standard deviations (modified) are factors of 10 ranging from one to a million exposures

The concept of "number of exposures" is incomplete without considering the whole triad of the *number* of exposures of a certain *duration* with an *interval* between the exposures. The temporal duration and interval may range from very small fractions of a second to an entire lifetime. We can accept seconds, minutes, hours, days, months, years, and lifetime as a scale that doesn't fit an easy mathematical computation, and it might not always be true. If we accept a mathematically consistent unit that is measurable, we get into unusual terms bearing unnecessary precision.

7., 8. and 9.) AGE AND PARTS OF THE BODY

The fact that the earth goes around the sun at a rate that bears a constant relationship to sand dropping through an hourglass makes no *a priori* demands that all two-day-old fruit flies are more aged than all one-day-old fruit flies. But, the astronomical event is one of our most rigidly established standards and since everything is related to it, naturally everything has a relationship to it. The biological truth is that animals are born first, then they get old, and then they die. We know of nothing that deviates from this pattern. Animals with similar characteristics do not all live the same length of chronologic time. But there are some similarities. Some humans have shorter lives than some cats, but in general humans have a longer life span than cats. It is well known that all humans live to be 72 years of age exactly (only true for Social Security purposes). There are actuarily more 12-year-olds than there are 72-year-olds. But we have an equal interest at any age, and can make the assumption that the average age of the human is 36 years with a standard deviation of 12 years. This means that all persons are born at 0 year of age (which is not true), and all die at 72 years of age (this isn't true either).

Even if we accept this gross assumption, it is not true that a particular group of cells in the skin of the foot has the same "age" as a particular group of nerve cells in the brain. Radiation might affect the whole body of a 36-year-old man; at the same time it is also affecting some very young lymphoid tissue and some very old red cells. One of the first observations made in radiotherapy was that when one mass of tumor was irradiated, another mass got smaller; therefore, the part exposed is not necessarily the part affected. When we speak of an age phenomenon, we have to consider a triad of "age," "part exposed," and "part affected." It is easy to compromise on a 36 year ± 12 year age for the total human body and relate these six period to 6 years ± 2 years for the cat. But the situation is much more difficult when trying to divide the body into pieces as they are affected by radiation. There are too many parts, too many widely varying characteristics. However, if we stick to a standard six divisions and keep each of these as something that has meaning as far as radiation exposure is concerned, then we can say that there is such a thing as total-body irradiation; if this is one extreme, then the other is the irradiation of an extremely small portion of the body known to be nonsensitive to radiation (the end of the toenail). This establishes the extremes. The not-quite-so-extreme divisions are, the exposure of a very large portion of the body that is sensitive to radiation (the whole trunk) and irradiation of a small portion of the body that is relatively nonsensitive (a finger). Next to the arbitrary mean is a small portion sensitive to radiation and a large portion insensitive to radiation. This gives us six divisons that follow each other in an order of importance. I don't know how to define these six pieces exactly. The definition of the sensitivity of a part is one of the essential items in radiation research. But if we don't try to be too precise in the definitions, then we shall usually be in agreement.

10., 11. and 12.) THE EFFECTS OF THE RADIATION

There is no good all-encompassing end point to describe the effects of radiation. We may use death in whole bodies, but this does not apply to portions of the body or to nonliving whole bodies. Morbidity is undoubtedly more important, but except at the extremes, there is no easily definable point at which you can divide "yes" from "no." The problem of determining "how much effect" is a reason for doing an experiment.

It is probably necessary that an end point be determined separately for each problem. If we use some "lethal dose for the whole body" when we are discussing a population, this is one end point that is easily understood and applied. We can compare this with "no noticeable effects whatsoever." A less extreme end point would be where all get sick but all do not die. It is too easy to make a mistake because of an unusual event or a mistake in measurement, and so usually the LD_0 is really an LD 1 per cent or 2 per cent. The MD_{100} (morbidity dose) is really an MD 98 per cent or 99 per cent. We really mean that, for all practical purposes either *none* or *all* the animals are affected. At the lower dose end of the scale we may distinguish between *few* or *many* getting sick at some specified time.

With six separate classifications similar to six standard deviations, in an order of ascending severity, we have a scale for all measurements. But the effect (especially in populations) is of little value unless a time after the irradiation marks another end point for considering the end point. For example, the LD_{50} is meaningless unless it is plainly stated as a 30-day LD_{50}, or a 50-year LD_{50}, or a 1-minute LD_{50}. Eight hundred rads (or maybe even more) is a 30-day LD_{50} for the human population exposed to radiation, but it is not a 1-day LD_{50}; nor is it a 1-day LD_0. A dose of a million rads of radiation may be a 1-min. LD_{100}.

The time of occurrence after irradiation and the amount of effect depends wholly upon the state of health of the organism. A sick person will probably succumb to radiation at a much lower dose than a person in full health. Without being too precise we can establish six levels of sickness or health ranging from sick, grossly sick, to moderately sick, to moderately healthy, to good health, to healthy.

One 12-Dimensional Characterization

Table II summarizes the end points for each characteristic. Each of these 12 separate characteristics has one dimension. The same 12-dimensional picture fits exposure to any object. Even a Geiger-Müller tube responds to radiation according to a pattern of about 12 characteristics. It has limitations in dose, rate, energy, number of radiating events, and their duration and interval. A Geiger-Müller tube has an age and a state of health, but not quite in the same human body sense. Some parts are more susceptible to exposure than others.

We can draw a two-dimensional graph to illustrate each of the characteristics mentioned. But I don't know how to draw a 12-dimensional graph, which is what we are really trying to do. I can draw four three-dimensional graphs to show that every kind of radiation exposure can be distinguished in one way or another from every other kind of a radiation exposure. The first three characteristics, for example, relate to the dose of radiation; the second three relate to the time during which radiation is being applied; the third three relate to the exposure of the body; and the fourth three relate to the effect of the exposure.

But these are not 12 separate graphs; they are all one graph separated and separable only for convenience.

TABLE II

END POINTS FOR SIX CLASSES OF TWELVE CHARACTERISTICS

(ARBITRARILY ASSUMED FOR THE HUMAN IN A SIMULATED STANDARD DEVIATION)

CHARACTERISTIC	EXTREME -3σ	-2σ	-1σ	Mean $\bar{x}$	$+1\sigma$	$+2\sigma$	EXTREME $+3\sigma$
1. Dose	0	250	500	750 rad	1000	1250	1500
2. Rate	$<10^{-6}$	10^{-5}	10^{-4}	10^{-3}r/sec	10^{-2}	10^{-1}	>1
3. Energy	α	β	<100 kev X	>100 kev X	>1 Mev	>7 Mev	Bev
4. Number	1	10	100	1000	10^4	10^5	10^6
5. Duration	>Sec	minute	hour	day	month	year	life
6. Interval	"	"	"	"	"	"	"
7. Age	0	12	24	36 yrs.	48	60	72
8. Part Exposed	very small insensitive part	small insensitive part	large insensitive part	small sensitive part	medium sensitive part	large sensitive part	total body
9. Part Affected	"	"	"	"	"	"	"
10. Effect	no effect	$_1MD_2$	$_1MD_{50}$	$_{30}LD_{50}$	$_1MD_{100}$	$_{30}LD_{90}$	$_{30}LD_{100}$
11. Time	>Sec	minute	hour	day	month	year	life
12. Health	sick	grossly sick	moderately sick	questionable	moderately healthy	good health	healthy

THE THREE-DIMENSIONAL PRESENTATION

In Fig. I the first three characteristics are placed upon a three-dimensional coordinate system. The total dose in rads is put on the vertical coordinate. On the A (Vertical) Axis there may be either a very small amount of radiation (minus) or a very large amount of radiation (plus).

The rate at which the radiation is applied may either be very slow (minus) or very fast (plus). This is put on one horizontal coordinate (B Axis). On the other horizontal coordinate (C Axis) we may put the energy of the radiation in something that is most easily expressed as a tenth-value layer (TVL). You may have either a very low penetration (minus) or a very high penetration (plus). It doesn't matter how these coordinates are arranged so long as we follow an easily understood arrangement.

Since there is no real zero and no real maximum number for any of the characteristics, we can arbitrarily assign values to each corner of a cube as shown in Fig. I. Thus, corner number 1 is a plus plus plus (+++) corner, the highest possible dose with the fastest possible rate of the most penetrating kind of radiation. Corner number 8, on the other hand, is a minus minus minus (— — —) corner, the lowest possible dose at the slowest possible rate with the least possible penetration. Since we shall divide the scales into six parts each, there will be 216 subcubes illustrating these many rough characterizations of possible radiation dose. With an infinite number of points along each scale, there are an infinite number of possible kinds of radiation with just these three characteristics.

DOSIMETRY

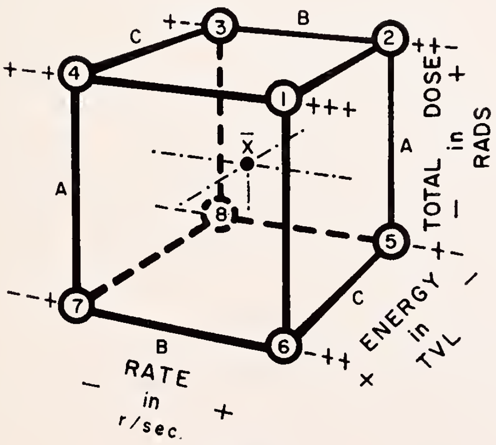

FIGURE I

I Dosimetry—Three of twelve dimensions on a three dimensional axis with the ends closed to make a cubical graphic presentation. See description in text.

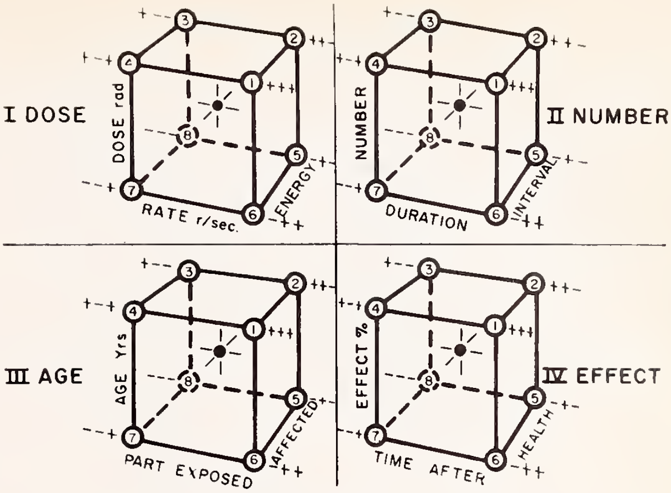

FIGURE II

All twelve dimensions on four three-dimensional cubical graphs.

In Fig. II all 12 dimensions are shown on four graphs. Figure II-I is the same as Fig. I. In Fig. II-II the second three sets of characteristics are on a similar three-dimensional cube, but there are some impossible points. On the first (Fig.II-I) cubical depiction it is possible to conceive of a very high dose at a very fast rate with an extremely high penetration. But (Fig. II-II), we cannot conceive of a large number of exposures with both a lifetime duration and a lifetime interval. Fig. II will be adopted as a conventional arrangement.

Table III lists 6 kinds of radiation exposure using only the grossest measurements of the characteristics. These are plotted on the 12-dimensional graph (four three-dimensional graphs) in Fig. III. Actually, using only the grossest measurements, there are well over 1500 kinds of exposure. If we were to measure the actual dose, or the actual rate, or the

TABLE III

THE GROSS CHARACTERISTICS OF RADIATION EXPOSURE

(Extremes are Assumed for Illustration)

(+ = large; — = small; ± = either; A = average)

EXPOSURE	I DOSE			II NUMBER			III AGE			IV EFFECT		
	Dose	Rate	Energy	Number	Duration	Interval	Age	Part Exposed	Part Affected	Effect	Time	Health
A Accidents	+	+	±	—	—	+	±	+	+	+	—	±
B Incidents	—	+	±	—	—	+	A	+	+	—	A	+
C Backgrounds	—	—	±	—	+	—	±	+	+	—	+	±
D Occupational	—	—	—	+	—	—	A	+	+	—	+	+
E Diagnosis	—	+	A	—	—	+	±	+	+	—	+	±
F Therapy	±	A	A	—	A	+	+	A	+	+	A	—

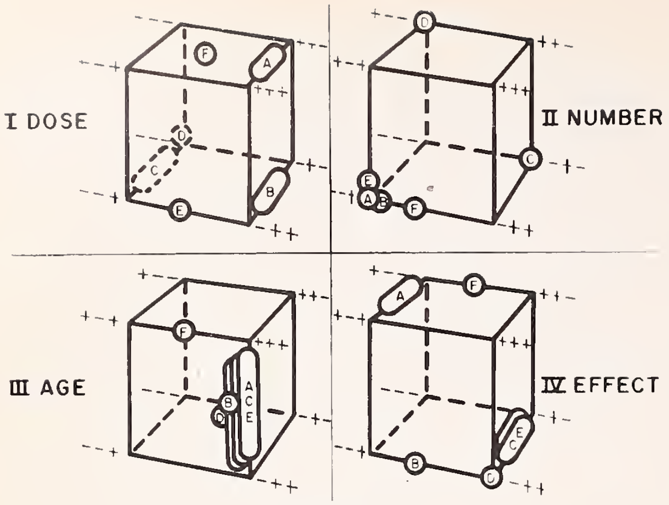

FIGURE III

The same graphs as in Fig. II except that six different kinds of radiation events are shown in their extreme positions. A = ACCIDENTS, B = INCIDENTS, C = BACKGROUNDS, D = OCCUPATIONAL EXPOSURES, E = DIAGNOSTIC EXPOSURES, F = THERAPEUTIC EXPOSURES.

actual age, to the fractional second, there are really an infinite number of kinds of radiation exposures—too many to consider. But we can think about the entire field in six groups.

There can be ACCIDENTS (A) involving radiation. There can also be INCIDENTS (B) involving radiation. An accident is defined as an event followed by hospitalization for other than public-relations reasons. An incident is an event primarily involving public-relations pandemonium.

There are lots of different kinds of BACKGROUND (C). There are also OCCUPATIONAL (D) exposures, which may or may not have some effect on the person so occupied. There are DIAGNOSTIC (E) and there are very different THERAPEUTIC (F) exposures.

ACCIDENTS AND INCIDENTS

By plotting a radiation accident (whether it is a political bomb or a technique mistake) we can see how the four three-dimensional graphs are used. For example, in Table III and Fig. III, an accident (A) is characterized by a high dose of radiation, a very fast rate, and either high or low energy. On the graph labeled III-II, there is only one position. The exposure may be of very short duration, and the interval may be long. At this point we can get into some difficulty. If, for example, there were a number of explosions, the duration of each would still be very short, but the interval between each exposure might be very short or very long, but it could not be a lifetime interval.

On the III graph in Fig. III, an accident can affect a person of any age. The total body is exposed and the total body is affected. On the IV graph, an accident will probably have a very large effect on the person so exposed. It will show this effect a short time after exposure; it can affect people in any state of health.

An incident (B), Fig. III, is entirely different; for example, an atom bomb falling in a plane crash but not detonating. This incident has occurred and we have considerable evidence as to what will happen. There is a low dose. Most of the energy of the radiation that does affect a human is purely alpha particles external to the body, the rate is fast. The number of such events is small as far as the exposure of any one person is concerned. If there is any internal exposure at all, the particles absorbed will be excreted from the body. Thus the duration is days and the interval will be long. In graph III (Fig. III), the age is indefinite but probably will be of persons free to move about and hence infants and the aged will be excluded. The part exposed might be the total body and probably would be, unless there was a missile injection in which case the part exposed would be small. The part affected is probably total body even if the part exposed is small. However, as shown in IV (Fig. III), the amount of the effect is exceedingly small and what effect there is probably occurs months after exposure. It probably affects a person in good health.

Most accidents are characterized by high dose and rate and either high or low energies. Most incidents, on the other hand, are characterized by low doses, high rates, with either high or low energies. The other factors all tend to be similar, except of course for the amount of effect. A person exposed to a very high-dose accident develops a great effect. A person exposed to a very low-dose incident develops almost no effect. This can lead into a difficulty. For example, there may be a great effect caused by incidents, if we consider the psychological effects as a kind of disease. In the Houston incident, even though there was a very low dose and physicians could detect no discernable clinical effect, there was a great effect not only on the person involved, but his entire family. Any person so affected might be sick to begin with, but such matters cannot be generalized. The distinction between an accident and an incident here has to be in the I depiction of characteristics and not in the IV depiction

INCIDENTS AND BACKGROUNDS

Both incidents and backgrounds have low dose in common. However, the rate of exposure is usually faster in incidents and slower in backgrounds. This may be confused by our definitions; if we consider a single cosmic ray as a single exposure, then its rate is high. Even this similarity is separable in the II graph where incidents tend to be few, whereas the number of cosmic rays is large.

BACKGROUNDS AND OCCUPATIONAL EXPOSURES

Occupational exposures are low-dose events just like backgrounds; if we went to a finer measurement, the occupational exposure would probably be noticeably higher than backgrounds. And so there is already a distinction, but sometimes these distinctions are difficult to make. For example, a room-background is similar to a uranium-ore mining measurement. In the gross sense, the doses are both small; but usually in a finer measurement the dose in an ore-mining operation is larger than ordinary background. However, the age of the person exposed might be very different. Every person of any age is exposed to background radiation. Only during the working years are persons exposed to a mining operation. In situations where there is a great similarity, the gross characteristics do not easily separate kinds of radiation exposure.

DIAGNOSIS AND THERAPY

Diagnostic and therapeutic radiations are easy to separate from other kinds of exposure if only because diagnostic and therapeutic procedures are purposely applied at a definite time. However, these diagnostic and therapeutic exposures do fit in with an attempt to describe the characteristics of radiation exposures. Diagnostic radiations are always low dose. Therapeutic exposures are always high dose. Diagnostic exposures may be applied to either healthy or sick people; therapeutic exposures are always applied to sick people. There is usually no radiation effect from a diagnostic exposure; there is an intended effect in a therapeutic exposure.

Examples

The utility of characterizing a radiation event is illustrated by a few examples. Figures IV, V, and VI are each drawn in two halves. The left-hand half is the four boxes similar to Fig. II which show the kind of radiation event that is being spoken of.

Any three characteristics may be taken to illustrate a point, and the cube is turned to give the most understandable view of the three-dimensional surface that results. None of these examples are known to occur according to the surfaces shown on Figures IV, V, and VI. These are all made up from many different observations (most not even in humans). In most radiobiological observations the characteristics chosen, the scales used in measurement, and the conditions of radiation are not measured and so it is impossible to make comparisons.

In Fig. IV, an ACUTE LETHAL EXPOSURE in humans is described. The dose ranges from 0 to

ACUTE LETHAL EXPOSURE

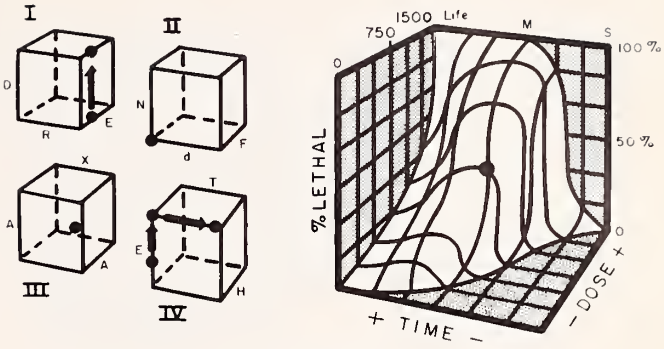

Figure IV

ACUTE LETHAL EXPOSURE in humans depicted on a three-dimensional surface. On the left the four cubical boxes show that the dose ranges from very low to very high dose, but is at a very fast rate and for a medium-high energy. The II graph shows that only one exposure of very short duration and very long interval has been selected. On the III graph, it shows that the age of the human chosen is a medium age, the total body is exposed and the total body is affected. On the IV graph, it shows that lethality from a small portion to a large portion of the population has been selected as the effect varies from seconds to a lifetime. The patient is assumed to be healthy. On the right, a three-dimensional surface has been depicted. Notice that the positioning of the graph is not necessarily that shown on the left series of graphs.

CHRONIC LETHAL EXPOSURE

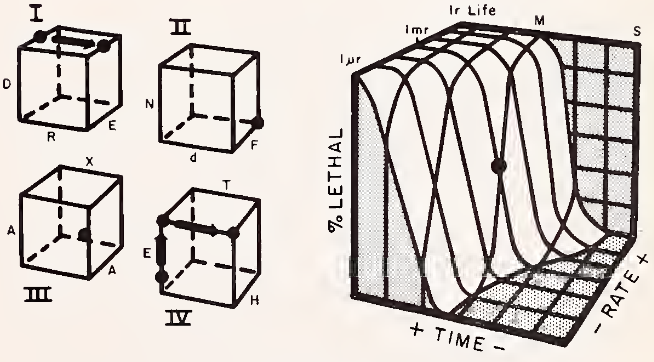

Figure V

CHRONIC LETHAL EXPOSURE in the human is depicted. On the left, the I graph shows that the dose is always chosen at an extreme level, but that the rate is varied from slow to fast. The energy is at a reasonably high gamma-ray energy. In the II graph it shows that only one exposure of very long duration and a very short interval is chosen. The III graph shows that a medium age has been selected with a total body exposed and a total body affected. The IV graph shows that lethality is one of the parameters considered and the time after irradiation that the effect takes place ranges from a short to a long time. A healthy person is assumed. On the right, the three-dimensional surface for this kind of exposure is depicted. It is entirely different from the three-dimensional surface for an acute lethal exposure.

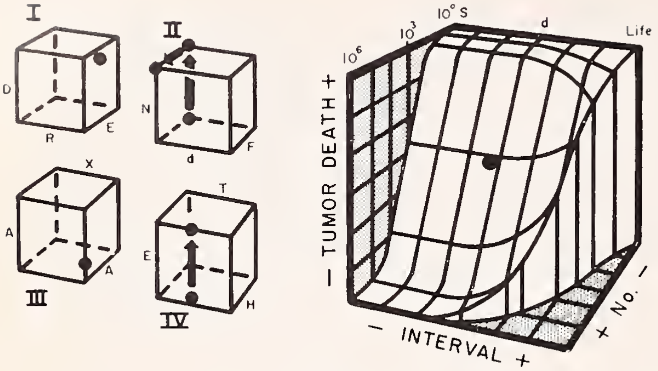
LETHAL TUMOR FRACTIONATION

Figure VI

A LETHAL TUMOR FRACTIONATION is depicted. Note that here it is the population of tumors rather than the population of humans that is examined. The I graph on the left, shows that a high dose, fast rate, and reasonably high-energy gamma ray have been selected. The II graph shows that the number of exposures ranges from a small to a large number. The interval changes from a short to a long interval. The duration of each exposure is short. The III graph shows that a fairly young age (of the tumor) has been chosen and the total tumor is both exposed and affected. The IV graph shows that the effect ranges from nothing to lethality in the whole population of tumor cells. Thus, there can be a partial death for the tumor as a whole. The time after exposure that the effect takes place is taken as approximately a month. The tumor cells are assumed to be healthy (as tumor cells). The right hand graph shows the surface that might result. This may not be correct because this is one of the items for research.

1500 rads. At 0 rad there are no deaths, at 1500 rads all humans die. The time of death might be different at different doses. It appears that at the higher doses death occurs in a shorter period of time following the acute exposure. At the lower doses, death occurs at a slightly longer time; but not all of the persons die. A high proportion may die in about a one-month period, but even at the same dose a lower proportion might die at a later period of time. The three-dimensional surface is therefore an irregular one.

In Fig. V a CHRONIC LETHAL EXPOSURE is illustrated. From the left-hand side of the chart it is seen that a certainly lethal dose has been chosen, but the dose rate is the important item and it is varied from a very slow rate to a very fast rate. At extremely slow rates it is impossible to reach the necessary lethal dose within the lifetime of a human, and therefore only a portion of the possible rates can be shown. At extremely high rates the chronic exposure tends to become confused with an acute exposure. The three-dimensional surface of a chronic exposure is entirely different from the three-dimensional surface of an acute exposure.

In Fig. VI a LETHAL TUMOR FRACTIONATION is illustrated. Here it is not the human that is considered, but rather the tumor itself. A specific dose, a specific rate, and a specific "energy" of radiation is selected. The number of exposures ranging from 1 to 1,000,000 is one item that is varied. The interval between these is another item that is varied, and the effect that is chosen for illustration is the death of the tumor itself. Implicit in the selection of these three factors is a particular duration that must fit the shortest interval, the dose rate, and all other factors. In order to define a radiation event it would be necessary to specify a definition for each of the factors that are important, and yet we don't know which factors are important. If, for example, we were to include in the characterization the number of Lysozym packets that were ruptured by the radiation, this might have an important bearing on the rate of vacuolation in each cell, and hence the cell death within the tumor.

It is impossible to think of all the things that should go into a definition. Therefore, we can only characterize and take the main items that will occur with the radiation of any object. This is the purpose of a radiation research project, to be able to compare one radiation event with another. There are so many possible kinds of events that no one person can do the entire job. Therefore, there must be a system for allowing the major characteristics of an exposure by one worker to be compared with other characteristics chosen by other workers. This is not yet being done in radiobiology, and hence the field is confusing rather than illuminating.

In Table IV, 36 different kinds of radiation events are compared. Six different kinds of accidents are compared with six different kinds of incidents, are compared with six different kinds of background, are compared with six different occupational exposures, are compared with six different diagnostic procedures, and all are compared with six different kinds of therapy. In actual practice the characteristics are not at the extremes as shown on Table IV. But in order to illustrate both the differences and the similarities between the various kinds of radiation exposures, we have to assume the most extreme situation.

For example, an atom bomb explosion (number 1 on Table IV) is very similar to a cyclotron exposure (number 2 on Table 4). It can be very similar in almost all respects except that usually the age of the person involved in an atom bomb explosion can be any age. Usually only middle-aged persons would be exposed to a cyclotron. The state of health can be either "sick" or "healthy" in an

Table IV

The Gross Characteristics of Some Exposures

(Many characteristics are not extremes, but we assume the most extreme situations for illustration.)
(+ means very large; — means very small; ± means either or both; M means midway.)

	I			II			III			IV		
	Dose	Rate	Energy	Number	Duration	Interval	Age	Part exposed	Part affected	Effect	Time of effect	Health
A. *ACCIDENTS*												
1. Atom-bomb explosion	+	+	+	—	—	+	±	+	+	+	—	±
2. Cyclotron exposure	+	+	+	—	—	+	M	+	+	+	—	+
3. Reactor accident	+	+	+	—	—	+	M	+	+	+	—	+
4. Klystron tube exposure	+	+	—	—	—	+	M	+	+	+	—	+
5. P^{32} ingestion	+	+	—	—	—	+	M	+	+	+	—	+
6. Plutonium processing explosion	+	+	—	—	—	+	M	+	+	+	—	+
B. *INCIDENTS*												
7. Plutonium leak from truck	—	+	—	—	—	+	M	+	+	—	M	+
8. A-bomb plane crash	—	+	—	—	—	+	M	+	+	—	M	+
9. Isotope transport truck crash	—	+	—	—	—	+	M	+	+	—	M	+
10. Houston iridium scare	—	+	+	—	—	+	M	+	+	±	M	—
11. Stolen Co pellet	±	+	+	—	—	+	M	+	+	±	M	+
12. Astronaut orbiting earth	—	+	+	—	—	+	M	+	+	—	M	+
C. *BACKGROUND*												
13. Body K^{40} beta-ray background only	—	—	—	—	+	—	±	+	+	—	+	±
14. Distant fallout	—	—	—	—	+	—	±	+	+	—	+	+
15. Room background	—	—	—	—	+	—	±	+	+	—	+	±
16. Body K^{40} gamma-ray background only	—	—	+	—	+	—	±	+	+	—	+	±
17. Cosmic ray electro-magnetic	—	+	+	+	—	—	±	+	+	—	+	±
18. Solar flare	—	+	+	M	M	M	±	+	+	—	+	±
D. *OCCUPATIONAL*												
19. Mining uranium ore	—	—	—	—	+	—	M	+	+	—	+	+
20. Dial painters	—	—	—	—	+	—	M	—	—	M	+	+
21. Isotope-processing technician	—	—	—	+	—	—	M	+	+	—	+	+
22. M.D. doing fluoroscopies	M	M	—	+	—	—	M	—	+	M	+	±
23. X-ray technician	—	M	—	+	—	—	M	+	+	—	+	+
24. M.D. doing radium therapy	M	M	M	+	—	—	M	+	+	M	+	—
E. *DIAGNOSIS*												
25. Tritium cytogenetics	—	M	—	—	—	+	±	+	+	—	+	+
26. I^{131} diagnostic test	—	M	M	—	—	+	±	+	—	—	+	M
27. Chlorine^{38} diagnostic test	—	+	—	—	—	+	±	+	+	—	+	M
28. Routine chest film	—	+	M	—	—	+	M	—	—	—	+	±
29. G. I. X-ray series	—	+	M	—	—	+	M	—	+	—	+	—
30. Placenta-previa search with I^{131}	—	M	M	—	—	+	M	+	+	—	+	+
						(baby)	—	+	+			
F. *THERAPY*												
31. P^{32} brachytherapy	+	M	—	—	M	+	+	M	M	+	M	—
32. I^{131} therapy	+	M	M	—	M	+	+	+	M	+	M	—
33. Radiotherapy	+	—	M	M	—	+	+	M	M	+	M	—
34. Radium therapy	+	M	M	—	M	+	+	+	+	+	M	—
35. Au^{198} ascites palliation	+	+	—	—	M	+	+	—	—	+	M	—
36. Direct injection of Y^{90} in prostate	+	+	—	—	M	+	+	—	—	+	M	—

atom bomb explosion, but there will usually be a healthy person involved in a cyclotron exposure. On the other hand, a cyclotron exposure and a reactor accident might be exactly similar in all respects when only the grossest characteristics are used. This is not true when the individual events are actually measured.

On the other hand, all incidents (the word "all" is used with trepidation) are different from all accidents. We can question whether an astronaut orbiting the earth (number 12 on Table IV) is exposed to a low dose or a high dose. At the same time we can question whether this is an accident or an incident.

Backgrounds and occupational exposures are different from accidents and incidents but they have some similarities that are in themselves items to be answered in a theory of radiation effects. The characterization of radiation is not simple and it will not get simpler as more kinds of radiation exposure are evolved. In going over Table IV, I have changed the designations of gross characteristics many times. When the actual measurements on common scales are substituted for the plus-minus gross designation, much of the confusion is resolved and even very similar radiation events are found to be entirely different from each other. When we consider that the measurements themselves are often highly suspect (measurements of dose in an accident) we see that it is impossible to define a radiation event; we can only characterize it. A system for reasonably uniform characterization is necessary. Twelve dimensions are insufficient, but there is a point beyond which confusion will supplant clarification.

Summary

In physiology the day of the Claude Bernard type of experiment is over with. If you chop off an animal's head, the animal dies. This is only true of some animals. It was necessary to perform the experiment where simple observations did yield an obvious answer. This is a "yes-no" type of experiment with an easy end point. The experiments were sometimes elegantly devised and are undoubtedly the best (and simplest) kind of science. But the day for doing this kind of experiment has long since past. The experiments had to be done only once and repeated a few times for verification. If they are ever repeated again they are for convincing students (which is not a waste of time), or are for fund raising programs (which does not fall within the realm of science).

In the same way, the day for talking about "radiation" is past. There is no such thing as an all-encompassing single characteristic event called "radiation," which can explain all mutants or no mutants, or can be characterized as all bad or all good, or can be described as entirely different from everything else, or exactly similar to anything else.

Radiation has many characteristics. The dose may be high or low, and this may or may not make a difference depending upon what is absorbing the dose. The rate of delivery may or may not make a difference. The energy of penetration may or may not make a difference. The number of exposures may be exceedingly high, but this may cause less effect than a single exposure.

There are 12 characteristics of radiation (at least) and they all range from small to large in an infinite series of points. Some of these characteristics might not even be definable even though the extremes are easily distinguished one from the other. We now have to talk about a multiplicity of types of radiation. We may find that some types are similar to other types. But we also know that some exposures are entirely different from others.

The Written Record

Whoever would make a due use of his attendance on hospitals must be at the pains of writing down the history of diseases and the method of cure, that he may have a fair view of the case after it is ended, and to fix it deeper in his memory. —William Heberden. *An Introduction to the Study of Physic.* New York, Paul B. Hoeber, Inc., 1929, p. 122.

II. Definition Of The Radiation Complex

B. The Sources Of Radiation Accidents

Marshall Brucer, M.D.

■ The sources of radiation accidents are all souces of radiation. Some, the natural sources, are unlikely to produce accidents, but they can; example, the dial painters during the early 1920's. Accelerators (X-ray machines are accelerators) are likely sources of radiation accidents. One would expect few accidents, but there are so many accelerators that, actually, they are probably the most common place for accidents. Nuclear bombs are thought to have the greatest potentiality for accidents, but there have been none. (The atomic bombs in Japan were not an accident; they were a deliberate explosion during wartime). Reactors, in spite of rigid safety controls, are a common cause of radiation accidents.

Accidents And Incidents

We have to approach a definition of the word accident. If we characterize a radiation event as either being *accident* or *incident, background* or *occupational, diagnostic or therapeutic,* then obviously diagnostic and therapeutic exposures are not accidents. They are deliberately planned events (although there can be accidents in these). Backgrounds and occupational exposures are deliberate in the sense that the risk is inevitable or we accept it

Accidents and incidents, on the other hand, are not deliberately planned. Although preparations can be made in expectation of their invevitable occurrence, we need some feature that distinguishes the accident from the incident. Probably the easiest is to say that in an accident somebody gets hurt and in an incident nobody gets hurt. This is a rather special definition. For example, a building that collapses with nobody in it may involve tremendous property damage, but it is an incident because nobody is hurt. A man burning his finger lighting a cigarette may involve little property damage, but it is an accident, because somebody gets hurt. The distinction is not always clear-cut. In 1957 an iridium tube was broken open, allowing a measurable contamination of a worker and his home. This is referred to as the Houston incident. The patient was alleged to have developed leukemia from exposure. He was treated by a physician for shock. The physician was alleged to have cured the alleged leukemia. Was this physician hurt by such therapy? His reputation certainly was. In which case, this is no longer an incident; it is an accident. Like all definitions, the accident-incident division is good only at the extremes.

Natural Sources Of Radiation

Cosmic rays are a natural source of radiation from which there is no escape. They probably originate as very high-energy photons in outer space. As these photons come through the atmosphere, the interactions of the extremely high energies may or may not cause many different kinds of transmutations into both heavy and light, short-lived and long-lived, secondary and tertiary, etc. particles that usually are (but may not be) absorbed in the earth's atmosphere. A person at a low altitude receives less of this radiation; a person at a high altitude gets more. In either altitude the dose to the body is exceedingly small (between 35 and 200 millirads) and so this is not a source for accidents.

There are periodic solar flares of radiation. Although these are spoken of as "tremendous" from the standpoint of physical insruments, they are insignificant to humans residing on earth (this might not be true for astronauts).

There is about a tenth of a microcurie of K^{40} in the human body (about 20 millirads per year). Even before it was known that the chemical potassium had a great deal to do with the normal functions of the heart, there was a serious attempt to explain heart action on the basis of the radioactivity from K^{40}. Potassium-40 probably never will be a health hazard, and even if it is, you can do nothing about it.

There is a little bit less than a tenth of a microcurie of C^{14} in the body. Strictly speaking, this is not inherent because C^{14} is manufactured probably by cosmic rays from nitrogen. In spite of its ubiquitous presence, it is not a source of accidents, although it is a source of radiation.

Although there is considerable variation in the relative importance of the natural radionuclides as sources of radiation, in their natural state they never constitute a health hazard. Most of the gamma radiation from natural materials is due to the presence of K^{40}, U^{238}, Ra^{226}, and other decay products from the heavier elements. (There are also some naturally-occurring radioisotopes in the rare earths.) Radon is a gas and can pervade local atmosphere. Local concentrations have been considered hazards. The accumulation of radon gas from the walls of some of the old houses in London was once considered a potential source of alpha radiation that might accumulate in the lungs and be a source of lung cancer. The ceaseless repetition of the Joachimsthal mine operations as a source of lung cancer is a statistical correlation that has never been proved, but it has never been disproved either. Radiation lung cancer has not been demonstrated in equally active atmosphere in South Africa.

During the height (1958) of the recent radiation hysteria, it was pointed out that the largest importation of radium into England was not under the name "radium." but of Brazil nuts. The monazite sands in southwest India have an accumulation of thorium far above that of other areas. People have been living in this high radioactivity level for many generations. There is no proof of injury; but again it is impossible to prove no injury. There is also said to be a South Pacific Island, and Brazil, and maybe many micro-areas that have a high accumulation of radioactivity.

Undoubtedly innumerable plants, animals, and chemical processes will result in a concentration of natural activities. These are likely called "tremendous" from the standpoint of measuring instruments. If these can ever be hazardous, they will be actuarial not individual accidents.

The purposeful accumulation of radium and similar materials for purposes of scientific study and medical therapy has resulted in some accidents. The radium-dial painters during the 1920's are the best known. It is not so well known that a much larger number of radium-dial painters went through the same process and apparently were not hurt. Von Schocky, the physician who invented (?) the luminous paint, died of aplastic anemia presumably from the radium he worked with. Even before the first World War, Giesel, one of the first German radium chemists was known to be extremely radioactive himself. (I don't know what the word "extremely" means and I don't know what he died of.) Even before 1900, H. Becquerel received a skin burn from carrying a small tube of radium in his waistcoat pocket.

During the 1950's, in Ohio, a company that was manufacturing ionization chambers used a small metal packet of powdered radium salt for calibration. Many uncalibrated chambers were placed in a circle around a central pneumatic device, which blew the packet up into position. It fell back into a protective storage pot upon release of the air blast. On one occasion the operator noticed a small puff of "white smoke" when he raised the source pneumatically. He tested it a couple of times and, since he got the puff of "white smoke" each time, he called his supervisor, who also tested it a couple of times, who called his supervisor, who also tested it a couple more times, who called his supervisor and finally by the time it was realized that this puff of "white smoke" was really powdered radium, the entire surroundings were contaminated. This was not a useless incident because it emphasized the necessity for never using pneumatic devices with any powered source even when supposedly sealed.

The discovery of the undesirability of pneumatic mechanisms was an experience of Leonard Grimmett, Ph.D., during the late 1920's. Dr. Grimmett, in a London Hospital, had just finished making the first really large teletherapy device. The five-gram radium source was stored in a heavily protected lead pot in one corner of the treatment room. The treatment device itself was in the center of the room and after positioning the patient the radiotherapist would transfer the source pneumatically from the lead safe to the teletherapy machine over a distance of many feet.

Five grams of radium was a tremendous source of radioactivity in the 1920's and expensive. It was borrowed from its Belgian manufacturers. One day there was to be a visit from the Belgian officials to view this remarkable and highly beneficial use of radium. Therefore the machine had to be thoroughly cleaned. A janitor in cleaning the device polished and oiled everything in sight. Dr. Grimmett had forgotten to mention that pneumatic devices must never be oiled. During the formal demonstration before the high officials, the source got stuck in the middle of the tube. Naturally the physicists had to unstick the source and get it back to a safe position. Dr. Grimmett was the physicist who got this job because it was too dangerous for anybody else. The same thing happened the second time, and Dr. Grimmett said he would never again design a device involving radioactivity that used a pneumatic mechanism.

Needles and tubes have been filled with radium for therapeutic purposes. These were "sealed" sources but not always completely "sealed," often they "leaked," but these events were not accidents; these were incidents. Also, radium needles got lost in cracks in the floor, down wash basins, or even in city dumps. Dr, Robert B. Taft, M.D., in 1938 wrote a book called *Radium, Lost and Found* describing his experiences—but again these were incidents, not accidents; but accidents did occur. Usually these "accidents" were connected with physicians loading sources repeatedly or placing them inside the patient surgically. The fact that these "accidents" were so frequent is one of the reasons why, during the late 1920's, the radiologic societies increased the tempo of their training program in radiation-hazard prevention. Such accidents are still occurring but now with almost negligible frequency.

Radiation From Accelerators

Probably the most common sources of radition that produce accidents are the various kinds of accelerators. An X-ray machine is an accelerator; cyclotron, vacuum tube, or a TV tube, all are accelerators. Anything that moves an atomic particle through a magnetic field and causes that particle to impinge upon a target or just changes its direction will produce some kind of radiation. The old-fashioned vacuum tube produced electrons by heating a filament with an electric current. The electrons were drawn toward the target with a magnetic field. The anode and even the grid inside some vacuum tubes are targets and X-rays are produced. But they are such low-energy X-rays that they are absorbed in the glass walls. A big linear accelerator might use any particle in a repeated series of reversing magnetic fields to reach enormous energies before finally hitting a carefully prepared target to produce almost any desired nuclear reaction.

Cyclotrons are a special kind of linear accelerator with the "linear" track curved in a different method of propulsion. Betatrons are a special kind of cyclotron that accelerates only electrons. The beams of radiation emanating from accelerators, and especially within the accelerators, may be at enormously high levels. Although the inventor of the cyclotron (E. O. Lawrence) preached radiation safety from the beginning of his project, some physicists did put their heads inside the beam to "adjust it." They developed cataracts. This was during the second World War, but more than a decade later some large klystron tubes were being repaired in a radar installation in New York State. In spite of warning signs the cap of the generator was removed with the machine in operation and the repairmen were exposed to partial-body radiation at very high levels.

Most accelerators are well protected against radiation exposure at this present date, but this was not always true. Also, there is a scattered radiation that results from every beam. The discovery of the present mode of producing C^{14} was almost accidental in that not much reaction was expected. Five-gallon carboys of rich C^{13} chemical were placed outside the useful beam of an early cyclotron. After many attempts to produce C^{14} by sophisticated target designs, Dr. Martin Kamen found a high production from the scattered slow neutrons outside the main beam.

Dentists used to hold film packs behind the teeth with one finger when a dental X-ray was being taken. After a few accidents occurred, this stopped. This sounds foolish now, but it wasn't foolish when it first started. It was natural for surgeons to set bones with the visual guidance of a fluorescent screen. The patient usually wasn't hurt by this procedure, but some of the surgeons developed severely ulcerated hands. As late as 1960 I saw a fresh radiation ulcer on the hands of an orthopedic surgeon.

Accelerators, and especially X-ray machines, were not always as well protected as they now are. Dr. E. W. H. Shenton writes in the *Archives of the Roentgen Ray* 6:63, *March,* 1902.

"I am assuming that you understand that the X-*ray tube is underneath the patient . . . I once had the good fortune to see an enthusiast lying on his back beneath the kitchen table on which lay a patient's leg, the tube being above all. The idea of reversing the positions of the operator and tube had evidently not occurred to him."*

Much of the current health physics literature seems to dwell with great glee on the horrible accidents caused by X-ray tubes; these are very old and well-known in the radiological literature. In a letter to the editor of the *Archives of the Roentgen Ray* 12:331, March, 1908 a knowledge of accelerator hazard is already implicit.

"To the editor: Sir,—At a meeting held at the Birmingham University on the 7th instant, presided over by Sir Oliver Lodge, a fund was started to assist Dr. Hall-Edwards, who is well-known as a pioneer in this country in radiographic work. (As a result of his work, cancer of the skin has developed in both hands. It has been found necessary to amputate one hand, and it is feared that he will lose the other.)"

Even before this tragedy occurred, Dr. Charles L. Leonard (*New York Medical Journal,* Nov. 16, 1907) called attention to the dangers of the roentgen rays. He stated that

"rules and limits of safety had been determined which rendered accidents rare, and the more serious are now only found amongst practitioners who are attempting to employ this powerful agent, whose potencies they cannot comprehend, with little theoretical and no practical knowledge or experience."

Accidents are rare where highly trained persons have been conditioned to radiation protection over many years of training. Accidents are less rare in industries where training and use are not so easily controlled. Very high-energy machines are special problems with enormous hazards that are usually well protected and carefully guarded; but where the possibility of an accident exists, Murphy's sixth law still stands: ultimately it will occur.

Atomic Bombs

If we discount the Japanese atom-bomb explosions, as deliberate not accidental, then the atom is the safest of all explosives; as yet there have been no bomb accidents. People have been hurt investigating bomb materials, but they have also been run over by automobiles during bomb transport. These are called automobile accidents, not bomb accidents.

When an unattached neutron enters the nucleus of U^{235} (or some other very heavy element), the nucleus becomes unstable and splits into two smaller parts that don't quite equal the mass of the original nucleus. The extra mass is released in the form of energy and more neutrons. If these new neutrons enter the atoms of other fissionable material, more fissions occur with the production of more neutrons. If there are sufficient fissionable atoms in the immediate vicinity, the process continues exceedingly rapidly as an explosion. This is the fission process and each of the smaller fragments formed is a fission product; it might be radioactive. Some of the energy produced is in the form of heat. Therefore, a fission reaction results in the production of fission products, neutrons and heat. The complete fission of about a pound of uranium or plutonium releases as much energy as the explosion of 8,000 tons of TNT.

In addition to the fission process, under conditions of extremely high temperatures two very light nuclei can be fused to form a single nucleus of a heavier element. This is referred to as a nuclear fusion reaction and because of the very high temperatures involved is called "thermonuclear." Such a reaction is also accompanied by the release of tremendous amounts of energy. For example, one pound of deuterium in a fusion reaction would release the energy equivalent of about 26,000 tons of TNT. The nuclei formed are usually not radioactive, hence the word "clean." In some kinds of fusion, neutrons of very high energy are liberated and these can in turn cause fission in other heavy-metal isotopes. This reaction produces an isotope (not radioactive) and neutrons of high energy. With both fission and fusion, the rapid reaction results in a blast wave. Since the only way to produce the tremendous heats necessary for a fusion reaction is through a fission reaction, both kinds of bombs result in at least some fission products. There is no "clean" bomb.

There are always some free neutrons in the air—about one per cubic meter. These usually result from cosmic-ray interactions in the atmosphere. These free neutrons have a half-life of about 30 minutes. If a free neutron enters the nucleus of a U^{235} atom there will be a "spontaneous" fission. If there is a sufficient number of U^{235} atoms in the same place (a critical mass) then the reaction can be self-sustaining; usually this does not apply. Spontaneous fissions release tremendous energy from the standpoint of one atom, but it is an awfully minute volume of effect. Spontaneous fusion might also occur. It is thought that the sun achieves its energy by a process of fusion.

The basic difference between a chemical explosion and a nuclear explosion is that the nuclear event produces millions of times as much energy in the form of thermal radiation.

About 50 per cent of a fission explosion is noticeable as blast; about 35 per cent is noticeable as a wave of thermal radiation. (About 45 per cent of a fusion reaction is thermal.) Only about 5 per cent of total fission energy is in an initial wave of nuclear radiation. Another 5 to 15 per cent results in residual or delayed nuclear radiation; much of it due to the radioactivity of the fission product. The initial nuclear radiations are mainly gamma rays of high (a few Mev) energy. These travel at the speed of light as an expanding sphere. The intensity decreases as the square of the distance from the point of explosion.

The neutrons initially produced are also of high energy, but their energy is rapidly dissipated into a full spectrum. These neutrons, like any others, can produce transmutations in whatever element they happen to meet up with to produce radioactive isotopes. The residual nuclear radiation is mainly due to radioactive isotopes so formed. Since elements are highly reactive chemically, they form chemical compounds—oxides and carbonates—and the radioactive isotopes actually exist as a "dust" that is carried upward by heat, outward by blast, downward by gravity. The dust can be washed out of the atmosphere and so we have such things as *fallout* and *washout* or *rainout* or *snowout*. They may be transported over long distances or come back to the earth in a short distance. If there is a "local" fallout, usually there are more radioactive isotopes in the fallout cloud and it is more dangerous. "Distant" fallout (distant here means thousands of miles) is spread over a very wide area and decays over a longer time; it is not dangerous. The accumulated dose to a human from distant fallout from all the bombs that have so far exploded is in the same order of magnitude as background radiation. Local fallout, on the other hand, can be at enormously high levels and might be very dangerous.

Nuclear explosions are of many kinds: air bursts, high-altitude bursts, (in excess of 100,000 feet), underwater bursts, underground bursts and surface bursts. A description of what can happen is not simple, but most of the complexities are variants of what happens to the fireball.

When a nuclear weapon is detonated, within a small fraction of a second a large amount of energy is released in a small area. The temperature inside this initial small fireball exceeds many millions of degrees centigrade. This compares with a few thousand degrees in a conventional high-explosive weapon. The great heat converts everything in the area into gaseous form. This also means that there are millions of times the atmospheric pressure.

Within a millionth of a second, the extremely hot gases radiate large amounts of energy as X-rays. These are absorbed by the materials (air, water, earth) surrounding the fireball and the ball becomes a hot, brilliant, spherical mass of gaseous residue. The luminous mass increases in size rapidly to more than a mile in a few seconds, but if it can, it rises like a hot-air balloon and as it increases in size it cools off. After a minute, it no longer emits visible radiation. The expanding pressure wave leaves a vacuum in the center that is filled by sucking up materials from the outside (vapor, dust and debris); as it increases in size it also cools and the vapor is condensed. In a high-altitude burst, the fireball is large because the more energetic X-rays travel long distances before they meet a molecule of air. In an underground burst, the fireball is small. If the fireball is on the surface, it may create a deep crater and suck up tremendous amounts of debris. If it is on the surface of ocean water, both the sodium and the chlorine become intensely radioactive. If the fireball just barely touches the earth, there may be little or no local fallout (the Hiroshima bomb, for example). The Bikini explosion was over calcium carbonate; tremendous numbers of particles of unslaked lime became slaked by moisture, ranging from many microns to pea size, and moved in a cloud following the wind. The larger particles fell to the earth (the ocean) nearly 160 miles downwind; fell out 8 hours later, and looked like snow.

Immediately after the detonation, the wave of initial radiation is followed by a wave of high pressure. A shock wave and its accompanying wind moves outward at high speed. The wave of thermal energy, like the blast wave and the initial radiation wave, travels at high speed, but there is a very rapid falloff as more distance is covered. Also, heat is more likely to be attenuated than the initial high-energy radiation.

The heat wave is most dangerous immediately. Outside the fireball the thermal wave is hazardous for a much longer time, primarily because it can initiate additional fires that in themselves are sources of danger. The initial radiation is probably the least dangerous of the three. A significant danger might be the delayed radiation from radioactive fission fragments or neutron-activated bomb debris. These may exist as "throwout" close to (miles) the explosion, or as "washout" or "rainout" or "snowout" many miles from the explosion. It may also exist as gravitational "fallout" hundreds of miles or even as "distant fallout" thousands of miles from the explosion. The subject has many variables and is enormously complicated by the tremendous variety of effects.*

Since lots of neutrons are produced in the immediate reactions, it would be possible to surround the bomb or make the casing of something like cobalt. When the casing evaporated, neutrons would thus produce Co^{60}, a highly radioactive material; or the bomb casing could be made of gold to produce a highly radioactive Au,^{198} or tellurium could be used to make I.^{131} This is the origin of such things as the cobalt bomb or the iodine bomb. I don't think any military man would ever consider such an abortion, not because of the expense, but because it is largely uncontrollable, Military operations are at best risky and to spread a five-year half-life isotope in an uncontrollable fashion would restrict the weaponeer as much as the recipient. If it were possible to control the fallout, then a short half-life material such as Au^{198}, or Na^{24}, or Te^{131} might be feasible. Such bombs are probably purely newspaper talk.

The neutron bomb has also been played up in the newspaper. Such developments are highly secret and I don't know anything about them. However, when a large number of neutrons are available, they will cause transmutations and some of these will be radioactive isotopes. The production of other radiations is, of course, a possibility. Such developments are and should be closely guarded military secrets. We will hear about them after the next war. However, the medical problem will still be that of treatment of the acute radiation syndrome.

Nuclear Reactors

So many nuclear bombs are in existence that someday we are bound to have an accident, but there haven't been any as yet. Nuclear reactors are a different matter. In spite of the enormously complex safety precautions there have been some accidents; most not with the reactors themselves, but with the accompanying paraphernalia.

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* The subject matter is explained in detail in *The Effects of Nuclear Weapons* by Samuel Glasstone, USDOD, USAEC, April, 1962, Superintendent of Documents, USGPO, Washington 25, D. C., price $1.00.

HOW A REACTOR IS MADE

Nuclear reactors used to be called *piles* for a very good reason. The first reactor was a pile of graphite blocks surrounding a pile of uranium slugs. To be sure, it was a carefully arranged pile. Bombs and reactors are much the same thing with one big exception. Both are a mass of fissionable material wherein each fission produces enough extra neutrons to cause more fissions, thus causing a self-re producing chain reaction. The uranium atoms that are to undergo fission must be in the proper place so that the next neutron can reach them and this is what makes the big difference. The bomb is a self-limited reaction; after a sufficient number of fissions it explodes. The next uranium atom to be fissioned is forceably and suddenly moved away from the next neutron and the reaction stops. In a reactor, the next neutron to cause a fission is modified so that the reaction is *over* a self-sustaining level but *under* an explosive level. Achieving fail-safe control makes reactors complex; fundamentally, they are very simple.

A reactor can be thought of as a series of boxes within boxes. The first box is a mass of fissionable material. U^{235} is the only naturally occurring material that is fissionable with neutrons of low energy. U^{233} and Pu^{239} can be made from naturally-occurring thorium or U^{238}. Therefore, in the legislation involving atomic energy U,^{233} U^{235} and Pu^{239} are referred to as *special nuclear materials*. Thorium and U^{238} are referred to as *source materials*. When the special nuclear materials undergo fission, they give off high-energy or fast neutrons. These can't cause additional fission with the high probability necessary to sustain a reaction and so they have to be slowed down. The way to slow them down is by moderating their energy by letting them interact with some material that does not capture neutrons. Carbon is one of these materials.

Therefore, the second box surrounding the fuel is pure graphite called the moderator. None of the gamma rays formed during fission are captured by the light material forming the moderator and some of the neutrons even escape. Also, there are radioisotopes and fission fragments always being formed which themselves give off radiation that must be protected against. Therefore, around the moderator box, there has to be a shield. This is a box of very dense material and sufficiently fixed so that no radioactivity (or very little) escapes into the surrounding area.

But all the boxes are somewhat useless as they stand. The reaction must be controlled. Some holes have to be put through the shielding and the moderator boxes so that control rods can be inserted into the fuel box. These control rods are of cadmium or some metal that has an extremely high probability of capturing neutrons without undergoing a transmutation into a radioactive material.

The amount of heat inside the fuel box is tremendous. This must at least be removed and dissipated to keep the whole reactor from melting down. The heat can be used for producing steam that can be further used to produce power. But this means another series of holes from outside the shield to inside the fuel.

Sometimes the neutrons are wanted for other purposes. Another hole through the shield and moderator can be a "thermal" column. Sometimes it is desired to use some of the neutrons within the reactor box for the production of isotopes; this requires another series of holes. Each atom of fuel is used up once. The fuel must be periodically removed and recovered, reprocessed and reinserted.

The recovery of the unused uranium implies its separation from the used fuel, a chemical stew-pot full of well over a hundred different isotopes of almost all elements. Some of these are in high proportions, up to six to seven per cent of the total; others are in only a small fraction of one per cent of the total volume. Many are highly radioactive, some are useful. For example, I^{131} for a long time was produced primarily as a part of the fission product processing operation. Cs^{137} used in teletherapy is still a part of a fission product separation.

Some of the fission products could be an important part of the civilian economy. For example, Sr^{90} is an almost ideal source for low-power sources. Many of the radioisotopes are either present in small amounts or are nonradioactive and are in a highly impure form or too difficult (in terms of expense) to separate. Therefore, they are useless.

The unused fission products and certainly the useless materials bring up a serious waste-disposal problem. Even when the useful radioisotopes are removed from the waste there is still a highly radioactive material, in large volume, of long half-life that must be disposed of with reasonable safety. The simple fuel box within a moderator box within the shielding box becomes a sieve. Each penetration, although not a hazard in itself, is a *potential* source of hazard. Each process, from manufacturing the original components through recovery, reinsertion and waste disposal, is a *potential* source of hazard.

CLASSIFICATION OF REACTORS

There are many ways to classify reactors: civilian, domestic, or for export or as military reactors. We could classify them as experimental, prototype, commercial, or propulsion reactors. There are test reactors and teaching reactors. There are such things as critical facilities (reactors capable of sustaining a chain reaction, but designed for extremely low power). A simple mass of fissionable material of critical size and proper shape can itself be a "critical assembly."

Reactors may be designated as breeders or converters. Breeders are those that produce a second fissionable material identical to (in amount) or more than, the fuel consumed. More properly, a reactor that produces more of the same fuel is called a breeder, while that which produces a different fuel is a converter.

There are also such things as fast and slow reactors. Converting U^{233} from Th^{232} is more efficient with thermal (very slow) or slow neutrons; converting Pu^{239} from U^{238} is best with fast (high-energy) neutrons.

Thermal reactors have the advantage of using the smallest amount of fuel, but there is a disadvantage of the buildup of isotopes (xenon) that "poison" (have a greater probability of capturing neutrons than the fissionable materials) the reaction. An intermediate energy reactor eliminates this problem and uses a smaller amount of moderator. A fast reactor contains no moderator; therefore, it can be much smaller.

Another classification is to separate *homogeneous* from *heterogeneous* reactors. Homogeneous reactors are those in which the fuel, the coolant and, if necessary, the moderator are intimately mixed as a slurry and are continuously circulated from reactor vessel to recovery vessel. In the heterogeneous reactor, the fuel is in separate discs, or rods, or plates, or alloys, or ceramic pellets.

Another classification is one that only describes the coolant and how it is used. For example, there are *pressurized water* reactors or *boiling water* or *liquid-metal* or *gas* or *fused-salt* or *organic reactors.* Probably the best classification is the one that is also a description of the main characteristics.

An *aqueous, homogeneous reactor* is one in which uralyl sulfate is dissolved in heavy water (*aqueous*). The fluid is at one and the same time fuel and moderator and coolant (*homogeneous*). The liquid is pressurized to prevent boiling and is pumped through pipes into a reactor core of proper configuration and then out into a heat exchanger where steam is made. However, about a third of the radioactive fission products are gases of fairly long half-life and they must be removed. Also, the entire circulating fluid must be shielded because of its intense radioactivity. Also, there are some delayed neutrons and the entire piping might become activated.

In a *liquid-metal reactor* the uranium can be dissolved in liquid bismuth and this liquid becomes both coolant and fuel carrier. Bismuth has the advantage of permitting high temperatures. At ordinary pressures, a moderator must be placed around the core. Around any of the small-core reactors, a blanket of Th^{232} may be placed to use the neutrons leaking out of the core for conversion or breeding.

In a *heterogeneous pressurized water reactor,* the fuel is in metal-clad plates, and water as a coolant and moderator is circulated under pressure. In a *heterogeneous* boiling water reactor, various kinds of separate fuel elements are immersed in a tank of water, which becomes the moderator. If the water is allowed to boil, about ten per cent of the core volume is taken up by bubbles of steam; increased pressure adds an engineering complication. The steam may be used directly in a turbine to produce power, but there is also some gaseous nitrogen activity which means that not only the core but the entire steam-line turbine must be shielded.

Not only water but other organic fluids such as the perphenyls may become combined moderators and coolants in order to make an *organic moderated and cooled reactor.* There is an advantage in relatively small size and because of the absence of oxygen in the coolant, such as in the pressurized water reactors, there is no gaseous nitrogen activity and less shielding is needed. Perphenyls are non-corrosive, but they are subject to radiation damage.

In a *heterogeneous fast breeder reactor,* either plutonium or enriched uranium is used as the fuel. There is a blanket of depleted uranium (less U^{235}) surrounding the core. Since the desire is to use fast neutrons, no moderator is necessary. Usually liquid metals are used in order to minimize any moderation of the neutrons. However, plutonium is extremely toxic and so one of the chief problems is in re-processing to make new fuel elements.

There are *gas-cooled heterogeneous reactors.* Air is the gas and is drawn past uranium slugs, drawn through filters to take out the gaseous activities (for example, argon) and discharged through a high stack. The original Oak Ridge and Brookhaven reactors were air-cooled

There are *swimming pool reactors* in which an array of fuel plates is suspended in a pool of water acting as coolant and moderator. The operation of the reactor core can be watched; the thickness of the surrounding material is easily changed, and so it becomes a *shielding-study reactor.*

Probably the commonest names are pet names given by the designers. For example, the "Lady Godiva" reactor at Los Alamos was a bare sphere of fissionable metal. The "Clementine" reactor was in a canyon near Los Alamos and used Pu^{239} (code no. "49"). Initials of an official name have been used: the materials testing reactor is widely known as the MTR. The first reactor at Oak Ridge was, until finally shut down, the oldest reactor in existence and therefore was known as "Old Grandma."

REACTOR ACCIDENTS

It has been estimated that about five per cent of the cost and maintenance of a reactor goes into a subject that can be directly called "health and safety." Naturally, about half the cost is in making the process possible for a human to accomplish, but these have become accepted ways of operating and are not really safety procedures. For example, packaging and shipping 10 microcuries of I^{131} is really very simple. Pour a little fluid into a bottle. put it into a shipping container and mail it for a couple of cents postage. Ten microcuries of I^{131} can be completely ingested by any person without harm. However, because the problem is not just one shipment but an unknown number of multiples of 10 microcuries, and since the preparation is either from a target material or from fission products that might be intensely radioactive, everything must be done behind thick shields. The chemistry is complex; radiation as well as chemical purity is demanded, special labeling is necessary and special transport laws must be followed. In storage the package must be shielded. It has a short shelf-life. Therefore, the whole procedure is expensive. The safety precautions are probably all overdesigned, but common sense and safety in proper perspective of risk cannot be followed. Each incident involving radiation, let alone accident, is a field day for yellow journalism and timid political maneuvering. In spite of, and maybe even because of, the inordinate safety consciousness, there have been some reactor accidents.

ACCIDENTS, IN SOME WAY, CONNECTED WITH REACTORS

On December 1, 1942, after many months of work, 385 tons of graphite and 40 tons of uranium in the shape of 40,000 blocks, had been stacked into a pile called CP-1 (Chicago Pile No. 1). It looked like it would give a sustained chain reaction. At 3:35 p.m. on the 2nd of December, 1942, Enrico Fermi had the cadmium control rod pulled out, saw that a self-sustaining chain reaction was occurring, and had the control rod pushed back in. "We saw it was about as dangerous as crossing the street," said Dr. Norman Hillberry, one of the scientists in attendance at this first reactor operation in Stagg Field at the University of Chicago. And he was right. This reactor was dismantled in a few months and moved outside of Chicago to the predecessor of the Argonne National Laboratory where there were accidents involving other reactor designs, but not this one. The same idea was then transferred to Oak Ridge, Tennessee, where "Old Grandma," a similar design, was built and operated for more than twenty years without serious mishap.

The first "reactor" accident did not really involve the reactor itself. It occurred in Canada where one of the first reactors was installed (with pure graphite it would have been the first). The reactor waste was kept in a large tank off the ground. It tipped over and some of the highly active wastes were spilled out. There was some traumatic injury that demanded hospitalization and the entire area (including the hospital) was contaminated by people walking through the active wastes. Maybe this wasn't a real reactor accident, but the event was one of the necessary peripheral activities of reactor operation.

Fifteen years later, a fuel rod ruptured in one of the Windscale reactors on the west coast of England, just below Scotland. A "large amount" of radioactive effluent discharged through the stack. The major portion was radioactive particulates of Ru^{106}, Ce^{144}, Zr^{95} and Nd^{95}. There was a contamination of a large area of the Irish Sea, particularly the sea bottom, and about 400 square miles of land was "contaminated" with measurable amounts of activity. This was called "low-level" waste. The major worry was distinguishing measurable K^{40} and other natural activities from the fallout. The most newsworthy radioisotopes, Sr^{90} and Cs^{137}, formed only a minor portion of the effluent. This was not an accident, it was an incident. The major cost was in the improper public relations due to administrative ignorance and political committees. In the newspapers, I^{131} became the great bugaboo. The thyroid activity of thousands of children was measured. The Thames flowed white with dumped milk and many scientists seriously considered getting out of the business.

But the reactor engineers had never demonstrated what really would happen if a reactor did become uncontrolled under runaway conditions. The Spert (Special Power Excursion Reactor Test) reactor program was begun in 1954 at the National Reactor Testing Station in Idaho. The first deliberate runaway resulted in a mild muffled explosion, was completely contained within its own substance and automatically shut itself off. Almost 20 years (on July 24, 1962) after the first controlled chain reaction Spert IV achieved criticality. Since anything can go wrong, the object is to test everything. But the essential information concerning reactor accidents does not come from these tests. It comes from the unexpected; accidents that cannot be predicted.

Probably the first two "reactor" accidents occurred in August 1945 and May 1946. Even these weren't really reactor accidents. Two scientists were experimenting with "critical assemblies" composed of a core of fissionable materials surrounded by shielding material; heavy metal was used as a shield in the first accident, a less dense material was used in the second accident. The person conducting the experiment was touching the shielding at the moment of the reaction. Since the core was small and on a table, the reactions resulted in nonuniform total-body exposure. The hands and the arms received the largest dose, the abdomen and chest somewhat less, and the head and legs received the lowest dose. Other persons in the area were presumed to have received uniform doses of about one-half Mev neutrons (already considerably slowed down). They also received some gamma rays both from the initial reaction and from fission products. In all, ten persons received appreciable radiation. Two died, one on the ninth and one on the twenty-fourth day. Another showed signs of an acute radiation syndrome but apparently recovered completely except for bilateral radiation cataracts three years later. The other persons had no symptoms, but some minor hematologic signs.

In June 1952, four persons were in one of the reactor rooms in Argonne when the reactor was started up by mistake. (The mistake was that it was thought that all the people were out of the room.) No symptoms or signs referrable to radiation occurred and all four left the hospital after 16 days. There were some, though hard to find, hematologic changes.

Probably in 1953, two persons were exposed to neutrons and gamma rays from a "short general external" exposure because of a reactor accident in the USSR.

On October 15, 1958, six students were working with an experimental zero-power training reactor in Yugoslavia. The amount of heavy water in this natural uranium heterogeneous reactor was abnormally increased. The reaction was not immediately detected and the six students were exposed over an unknown number of minutes. There was a tremendous clinical investigation of the six persons. One died after all had been taken to Paris for further diagnosis and therapy.

On January 3, 1961, three armed forces men working with the SL-1 (Stationary Low Power Reactor No. 1) at Idaho Falls, were reconnecting the rod extension shafts in a reactor that had been shut down for 12 days for routine maintenance and installation of some experimental equipment. Two men were killed, presumably instantaneously, with evidence of the violent explosion within the reactor building. The third man died, presumably a traumatic death. All three bodies were intensely radioactive, presumably from both contamination and neutron-induced activities. The housing for the reactor was not even classed as a containment shell; it was not airtight, it was not blast proof, the doors were not tight fitting. In spite of this, there was very little radioactivity outside the reactor building.

There have been a few other "purely reactor" accidents. Usually they are not the fault of the machinery nor of human operating stupidity. Designers of reactors have so emphasized government control and reactor safety that they have added an overbearing check list of safety factor piled on safety factor so that natural human mistakes are easily forgotten.

ACCIDENTS INVOLVING MATERIAL PROCESSED FOR REACTORS

On June 16, 1958, In Oak Ridge, Tennesse, a mixture of uraniums went through a chemical processing. The waste materials were supposed to be (but were not) dumped into a container of safe configuration that could never become critical. The piping was supposed to be (but was not) clean. There should have been insufficient enriched residue. Twelve things had to go wrong in exactly the proper sequence and hence the accident was statistically impossible. The man filling the drums with reprocessing waste noticed an explosion and (luckily) ran. Four other persons were working on equipment in pairs (to prevent accidents) and received considerable exposure. Three others were at a distance and received minor exposures. The enriched uranium reached criticality in a liquid drum, the heat caused the fluid to boil thereby departing from the geometry necessary for criticality and so the reaction stopped. In stopping, the water got cool and the water again approached a proper geometric configuration. The reaction again started and stopped and started again and there was an "extremely rapid" series of critical reactions. Little contamination activity extended outside the immediate area, but there was considerable prompt gamma radiation measured by intruments a quarter of a mile from the source.

On December 30, 1958, an almost identical accident occurred. Residues of waste material were being processed for the recovery of plutonium; a routine operation carried out many times over many years and the tanks "never" contained enough plutonium at any one time to permit a critical reaction. When the accident occurred, an end-of-the-year fiscal inventory of fissionable material was being made and the normal flow through the reprocessing system was interrupted. The accident occurred shortly after the change in work shifts. The man who received the fatal exposure was standing over and looking into the processing tank. Two other chemical operators were in the immediate vicinity but received little exposure. The worker immediately affected received an enormous but nonuniform exposure.

Long before this, in 1953, a woman technician at Los Alamos was working with a plutonium solution as part of an investigation of processing procedures. A small amount of plutonium was in a glass flask that broke and the jagged edge of the contaminated glass cut across the base of her thumb through a rubber glove. There were a few "hot" spots after first aid cleansing. It seemed that little or no plutonium had penetrated into the body, but urine samples showed a measurable amount. A nonspecific malaise seemed to be related to the Ca-EDTA therapy even though it appeared to promote the excretion of plutonium. When treatment stopped, the signs and symptoms cleared quickly and in a few days the urine was entirely cleared and the patient appeared well.

Another patient had been working with plutonium for a number of years and had had several minor contamination accidents. The technician was working in a dry box used for processing plutonium residue. In placing a rubber tubing over the base of a suction flask the tip broke and he was cut over the ball of the thumb. The skin area was considerably contaminated with plutonium. The wound was surgically excised. Calcium-EDTA treatment repeatedly caused large excretions through the urine. It seemed that there was continuous feeding into the blood stream from an intramuscular source of contamination. A second surgical incision was made and, after a year, the urinary excretion had fallen to a very low level.

At about the same time in 1953, two young physicists were working with a 25-curie mock fission neutron source contained in a pile of graphite blocks. The neutron flux was higher than expected and so they investigated. The polonium-beryllium source had ruptured (apparently due to a buildup of hydrogen and oxygen from the radiation of moisture in the capsule) and sprayed alpha active materials over the entire room. There was no evidence of external injury. A shower and scrubbing with soap and water removed most of the surface contamination, but there had been some inhaled polonium. Treatment with chelates did not change the excretion rate. The two men never ceased normal activities, repeated out-patient hospitalization was for investigation, but after five months the excretion was still measurable.

On April 7, 1962, an excessive amount of plutonium collected in a container in a processing laboratory in Hanford, Washington. One employee was about 5 ft. from the container, some others were from 8 to 20 ft. away. They saw, rather than heard, an explosion, but immediately heard many safety signals and evacuated the building. Outside the building, a radiation monitor detected "probably-induced" radioactivity and the men were promptly sent to the hospital. Four persons had an easily measurable dose, but one dose was so low that the patient was immediately discharged from the hospital. There were no acute radiation symptoms in the three with the highest, but still low, dose and all three seemed well enough to be discharged in a few days.

There have been many other processing and waste-disposal accidents, but most are traumatic rather than radiation accidents. The radiation itself is incidental.

Isotope Accidents Unrelated To Reactors

There is a whole class of accidents not really related to the reactor, except they are either in close approximation to or the isotopes are used in the place of a reactor. The isotope is popularly (and wrongly) thought of as being a reactor. For example, in 1953 a very skilled radiochemist was working with an intense mixture of $Am^{241-242}$ and Cm^{242} (with, of course, associated fission products). These were in a quartz ampule. Just as the ampule was about to be opened it exploded. The contents were sprayed over the top of a lead shield into the radiochemist's face and hands. He immediately scrubbed thoroughly with soap and water, but there were still a few "hot" spots on his face. There were also minor abrasions. Laboratory tests in the hospital confirmed significant excretions. Repeated scrubbing of the skin and administration of chelate was the only therapy. The patient was ambulatory at all times. It was thought that swallowed contamination (much excretion is through feces) was causing an abnormal level in the blood and urine.

In 1961, a graduate student was irradiating materials with a 200-curie cobalt source. The source became detached from its usual holder and was in the student's hand for about 10 minutes. The student noticed a malaise, lethargy and nausea and vomited after four hours. He was hospitalized, but not until the 27th day of hospitalization did he develop some petechiae in the mouth. He did have a loss of hair. During the next year he went through a radiation-exposure disease.

There are hundreds of incidents that are alleged to be due to reactors which have no connection with reactors and are really not accidents. For example, on March 13, 1957, a Houston technician was exposed to a small amount of Ir^{192} contamination. A combination of newspaper sensationalism, a commercial protection firm's overwrought publicity hunger and very poor industrial advising caused this to become a major hysteria. During the first 6 months of 1962 a Canadian Co^{60} industrial radiography source became a toy in a Mexico City family. It is said to have (and might have) resulted in three radiation deaths. Most of the plutonium-contaminated metals are carried by truck from the Brookhaven National Laboratory on Long Island to and from Apollo, Pennsylvania. Sometimes there is a detectable contamination. In January of 1963 there was alleged to have been a leak from the truck on Long Island. There was said to be a "full-scale probe" by the USAEC even though nobody is known to have been harmed by the incident. There had been so many of these isotope transportation incidents reported (occasionally as serious reactor accidents) that official summaries of accidents and incidents have been published. Most of our knowledge of radiation exposure in the human is gained from the few real accidents that have occurred. No matter how undesirable the accidents are, they are laden with information and hence important to a physician.

Scientific Methodology

The theory of relativity is a fine example of the fundamental character of the modern development of theoretical science. The hypotheses with which it starts become steadily more abstract and remote from experience. On the other hand, it gets nearer to the grand aim of all science, which is to cover the greatest possible number of empirical facts by logical deduction from the smallest possible number of hypotheses or axioms. Meanwhile the train of thought leading from the axioms to the empirical facts or verifiable consequences gets steadily longer and more subtle. The theoretical scientist is compelled in an increasing degree to be guided by purely mathematical, formal considerations in his search for a theory, because the physical experience of the experimenter cannot lift him into the regions of highest abstraction. The predominantly inductive methods appropriate to the youth of science are giving place to tentative deduction. Such a theoretical structure needs to be very thoroughly elaborated before it can lead to conclusions which can be compared with experience. Here too the observed fact is undoubtedly the supreme arbiter; but it cannot pronounce sentence until the wide chasm separating the axioms from their verifiable consequences has been bridged by much intense, hard thinking. The theorist has to set about this Herculean task in the clear consciousness that his efforts may only be destined to deal the death blow to his theory. The theorist who undertakes such a labor should not be carped at as "fanciful"; on the contrary, he should be encouraged to give free reign to his fancy, for there is no other way to the goal. His is no idle daydreaming, but a search for the logically simplest possibilities and their consequences.—Albert Einstein. *Essays in Science.* New York, Philosophical Library, Inc., 1934, p. 69.

II. Definition Of The Radiation Complex

C. The Acute Radiation Syndrome*

Marshall Brucer, M.D.

■ Before he died in 1960, Dr. Gottwald Schwarz reminisced about the first studies of clinical radiation effects done with other students of the great German clinician and pioneer radiologist, Dr. Guido Holzknecht. Radiation therapy was already well started just after the turn of the century, sometimes with dismal failure. The physical and chemical effects were beyond understanding because even the simplest clinical effects were not straightforward; there were queer variations. The blood changes in humans were a question because the observations showed both stimulation and depression of the white cells; But there was dose dependence? – Dose-rate dependence? – Certainly a time-after-administration dependence. They tried to repeat their human observations in a study of dogs.[1]

Over a half century later, in 1959, after there had been a sufficient number of serious nuclear accidents, Dr. Thomas Shipman,[2] Health Director at Los Alamos, realized that clinical decisions had to be made despite radiobiological niceties. He decreed (with justification) that when the white cell count goes to 500 or less in the first 24 to 48 hours, there will be a grave prognosis. If the count remains above 1,000, we can be reasonably optimistic. This had been known to a small number of physicians for well over fifty years. It should have been known to every radiologist.

The details of diagnosis and therapy, and the interminable arguments on protection, rest with an understanding of the acute radiation syndrome. There will be modifications with chronic radiation and in the chronic syndrome. There will be changes and undoubtedly there will be re-emphasis if new information becomes available. But the third generation of physicians to be exposed to the problem should be able to argue with a clinical background. At least they should be able to do first aid.

The Levels Of Radiation (Fig. 1)

The range of radiation that might or might not affect the human being is from billionths of a rad (nanorads) to billions of rads (gigarads). The body itself, the food it eats and the earth it lives on, all have an inherent radiation measured in billionths of a unit. The old-fashioned and thoroughly unsatisfactory Maximum Permissible Dose allows an enormous safety factor. Most of the diagnostic radiations are in the rad level. In the kilorad level lethality to the human is almost certain. In th megarad level, radiation is lethal to most living things and the beginnings of large scale chemical effects are noted. In the gigarad level (billions of rads) almost everything we know is affected. Very roughly the range is from *background* through *tracer* to *diagnostic* to *therapeutic* levels of radiation. Beyond this there is *cellular damage, chemical damage,* and *damage* even to *metals.* It is probably true that all radiation that interacts in the body is damaging. However, this is the same as saying that all humans bleed. When they don't bleed, they are not alive; and where there is no radiation, there is no life.

The Three-Dimensional Presentation (Fig. II)

If we assume one short exposure to gamma rays, of short duration but long interval in a middle-aged man with the total-body exposed and affected and with the man in good health, we still have three variable parameters: the dose, the time-after-exposure that an effect is noticeable, and the amount of effect. All three seem equally important in making a clinical diagnosis. The diagnosis will have to be guessed at with or without adequate information. Figure II shows how a three-dimensional chart can be made that will illustrate what might occur (it is also necessary to illustrate how tentative such a summary is).

In Fig. II we are arbitrarily defining "acute" as sixty days. The effect is the total white blood cell count. Five cases were taken from the June 1958 Oak Ridge accident, and the white cell counts were averaged. They all received between 300 and 400 rads. Step 1 in Fig. II shows a two-dimensional graph of such an averaging. The statistics can be arbitrarily smoothed out to arrive at the picture shown in Step 2. After the exposure in these five accident victims there was a decline in the total white cell count. After a number of days the white cell count increased, and this is where Gottwald Schwarz in 1904 began his argument. Rather than continue the argument let us accept that there wa at least a leveling off and then during the third week, there was a further decrease. The leveling off (or increase) is an unfortunate and serious condition. Many physicians might get the idea that the acute radiation syndrome is finished and that this is the beginning of recovery. After a few weeks, however, the bottom drops out of the picture. About the fourth or fifth week, a true recovery begins.

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* *The substance of this paper has been presented at many Armed Forces Medical Symposia, Field Command, Defense Atomic Support Agency, Sandia Base, Albuquerque, New Mexico. It is a 1963 revision of USAEC Report ORINS—25,* The Acute Radiation Syndrome, *Office of Technical Services, Department of Commerce, Washington, 25, D. C., 1959.*

But this is true only at around 300 to 400 rads. We have to be interested in both lower and higher

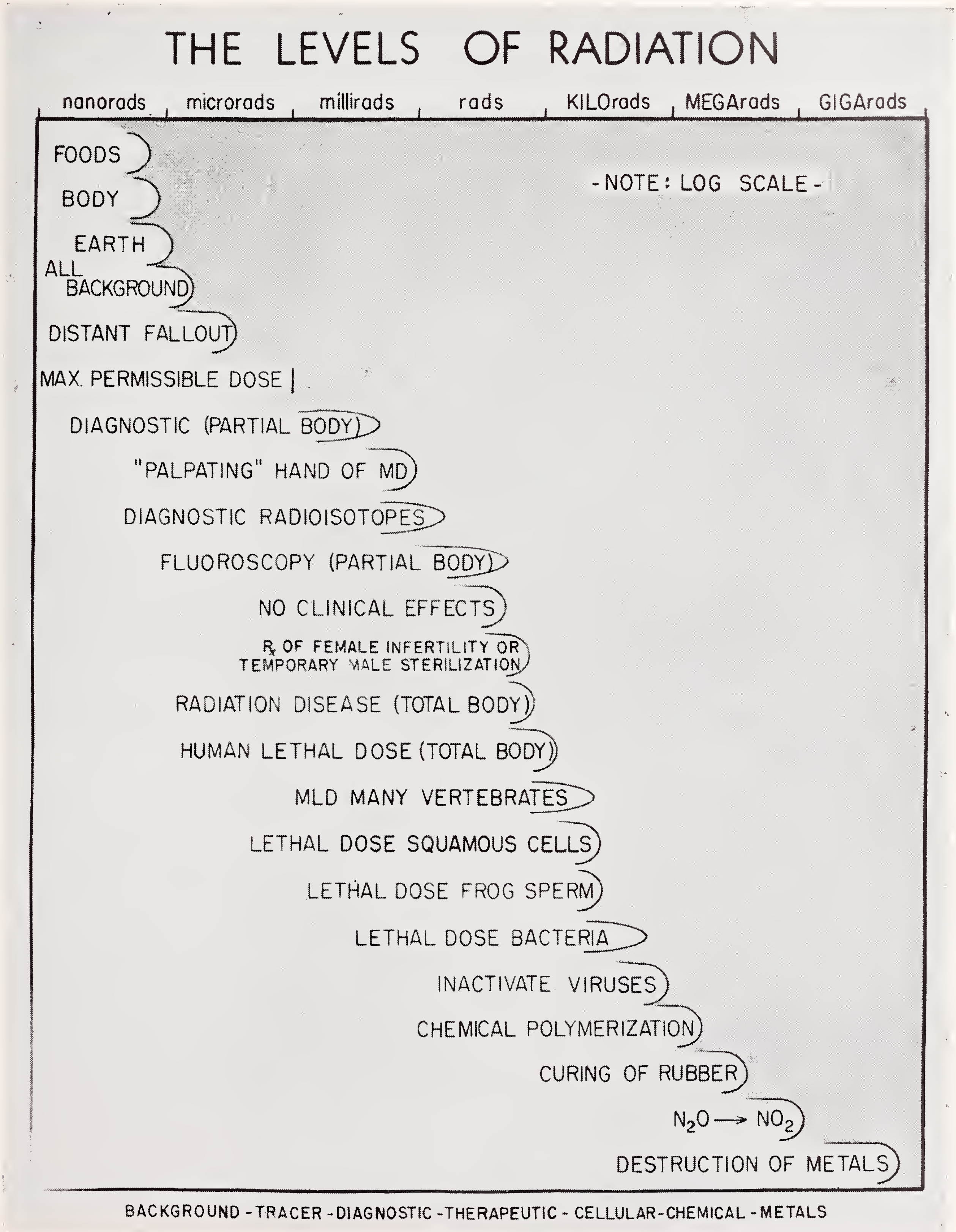


FIGURE I
The levels of radiation.

doses and here the picture might change. In Step 3 the smoothed two-dimensional picture is placed in its proper prospective in a third dimension of radiation dose. We have no evidence to fill in the rest of the dose ranges of interest. We do have evidence that at less than a few rads nothing occurs, and at more than a few thousand rads death intervenes before any white cell development can occur. Therefore, in Step 4 an extrapolation is made to all of the levels of radiation that are of interest to a physician.

Facts are not evidence unless some estimate is made of their reliability. In the lower left hand corner of each graph, a circle with some question marks will be placed. If there are two question marks, it is very probable that I don't know what I'm talking about. If there are three question marks, it is almost certain that you don't know what you are talking about either. The graphs are purposely made so that they cannot be read in detail. In the general picture all of the experts tend to agree; the arguments are on details.

The Significant Dose (Fig. III, No. 1)

Probably the first diagnostic guess the physician must make after the admission of a radiation accident patient is "what dose did he get and what dose is significant?" Lethality is only an index of the significance of the dose, but it is a good index. It appears that acute lethality is early—a matter of a few days—at the 1,000 rad level. Most (but not all) persons will die if they have received total-body irradiation at this level. Lethality is not so early—a matter of weeks—at a lower dose. It appears that lethality occurs in only a few people at levels above 100 to 300 rads.

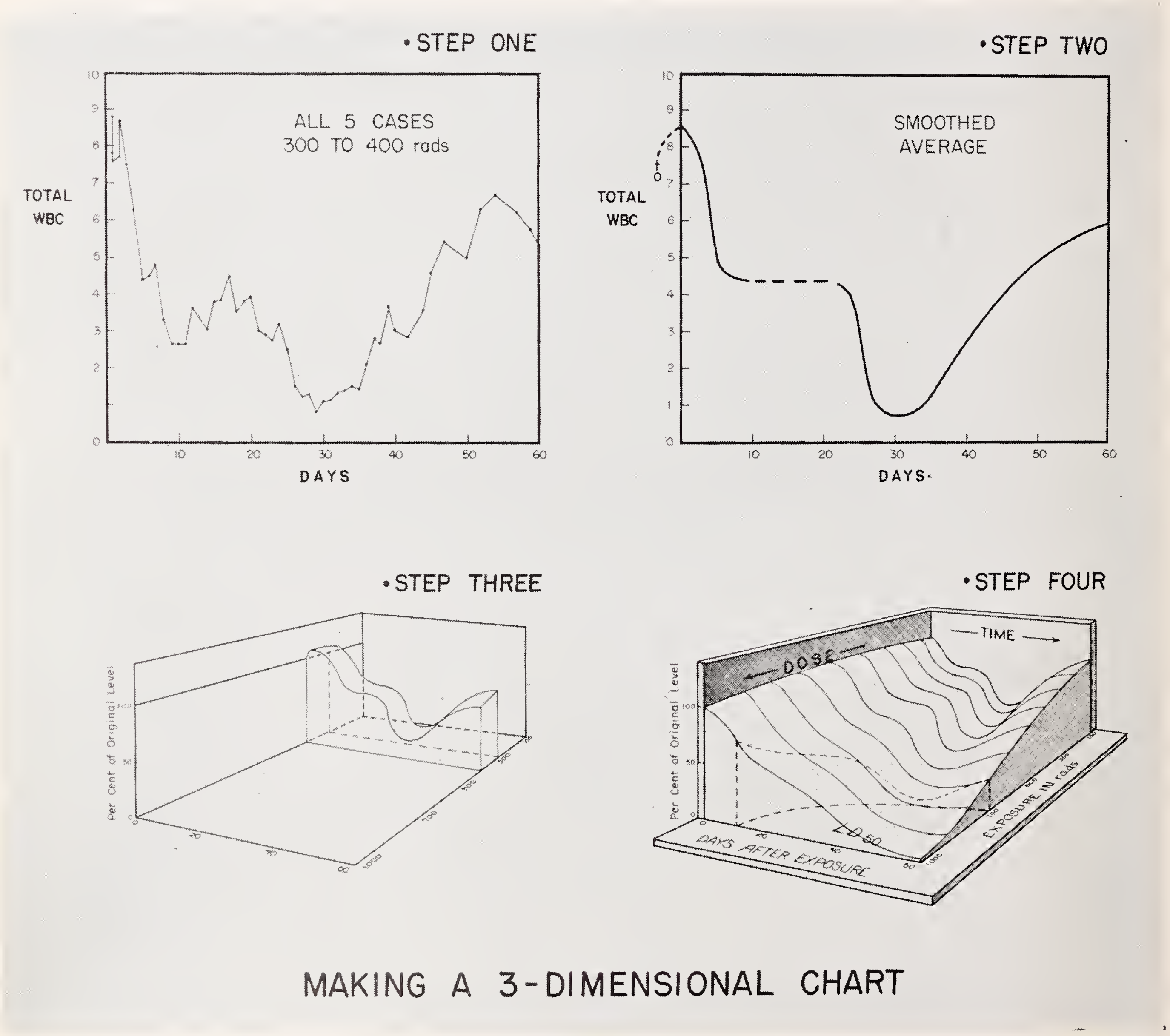


Figure II
Four steps in making a 3-dimensional chart; example: The total white blood cell count.

Fifty per cent of the population will be dead within a 60 day period after total-body absorption of about 700 rads (or 800 or 900; this is a detail for argument). There is some evidence that even the most rudimentary hospitalization will change this picture. A nonhospitalized LD_{50} dose for humans is probably lower than a hospitalized LD_{50}. The exposure is listed in the charts in rads; this is improper. Exposure by definition is in terms of roentgens whereas absorbed dose is in terms of rads. However, the physician making a diagnosis may have neither exposure figures nor a measured rad dose properly authenticated. Therefore, we are talking about a combination—a best guess at two inadequate calculations.

Vomiting (Fig. III, No. 2)

The practicing physician has a real interest in the medium-dose range (between a few hundred to a thousand rads). This is the range immediately above and below an acute LD_{50} for humans. Many people so exposed will recover, but many will also have aspects of their radiation disease that must be treated, albeit symptomatically. One of the first symptoms to make itself known to the physician is vomiting. Patients with large doses vomit early; with small doses, they will not vomit. It appears that vomiting at lower doses, when it does occur, occurs later than vomiting due to high doses.

Even this simple symptom is not something a physician can accept without scepticism. There are such things as psychogenic, iatrogenic and newspaper-ogenic vomiting.

The Lymphocyte Count (Fig. III, No. 3)

To almost every physician in the United States, a blood count is a routine procedure. It appears that at both low and high doses the lymphocyte count decreases with equal rapidity. However, at high doses, the count goes down farther than it does with low doses. While the fall in lymphocyte count is occurring, no interpretation of the decrease is possible except to inform the physician that radiation exposure probably did occur. If the patient does not vomit, but has a decreasing lymphocyte count, it probably means that he has been irradiated with a relatively low dose. If he is vomiting and the lymphocyte count continues to decrease, it probably means that there has been a higher dose. If there is no vomiting and no decrease in lymphocytes, the exposure of the patient to a significant dose is questionable.

Erythema (Fig. III, No. 4)

Erythema is more closely related to "energy" than "amount" of radiation. Lower doses of low-energy radiation are more likely to produce erythema than much higher doses of high-energy radiation. This is a symptom that has been talked about for more than sixty-five years among radiation experts. We know considerable about erythema from partial-body exposure. If it does not occur within the first few hours, it probably means that there has been a relatively low exposure. If it occurs almost immediately and is severe, it probably means that there has been a very high exposure. The position of the erythema on the skin is not a good index of the dose or direction of approach unless the physician knows the energy of the radiation. Very high energy radiation may result in an exit dose erythema.

Body Temperature (Fig. III, No. 5)

When a patient enters a hospital, nurses are trained to insert a thermometer into the first opening that presents itself. With very high doses of total-body irradiation, almost all patients will immediately develop a radiation-induced fever. This can be both symptom and sign. Patients have complained of the fact that they "feel hot all over." Patients who have received a much lower dose, but chronically *not* acutely, have developed fever that might have been radiation induced. Almost all patients with significant doses of radiation ultimately get some kind of minor infection; this in itself might cause a fever. The question of whether any specific fever is or is not radiation-induced is impossible to determine. The American experts in 1959 did not believe in a pure "radiation-induced fever." The Russians during 1959 did believe in a "radiation-induced fever." In spite of the arguments, it is probably prudent for a physician confronted with fever in a radiation accident victim to look twice for infection and then first to treat a nonspecific infection or second to treat the patient as though the fever were infection-induced. Mistreatment of a radiation-induced fever is probably less dangerous than no treatment of an infection-induced fever.

The White Cell Count (Fig. II)

There is almost certainly a double dip in the white cell count after a total-body irradiation. Leukemia is not a part of the acute radiation syndrome; however, the changes in the white blood cell count are entirely different when leukemia patients are irradiated than when normal patients receive an accidental exposure. It seems that the level to which the white cell count descends on its first dip is somewhat indicative of the dose. But, the variation is too great for diagnostic purposes. It is apparent that the timing of the two dips and the leveling off in the white cell count is about the same at all doses. The first dip occurs during the first week and the second dip reaches its low point at about the third week. Recovery from the second

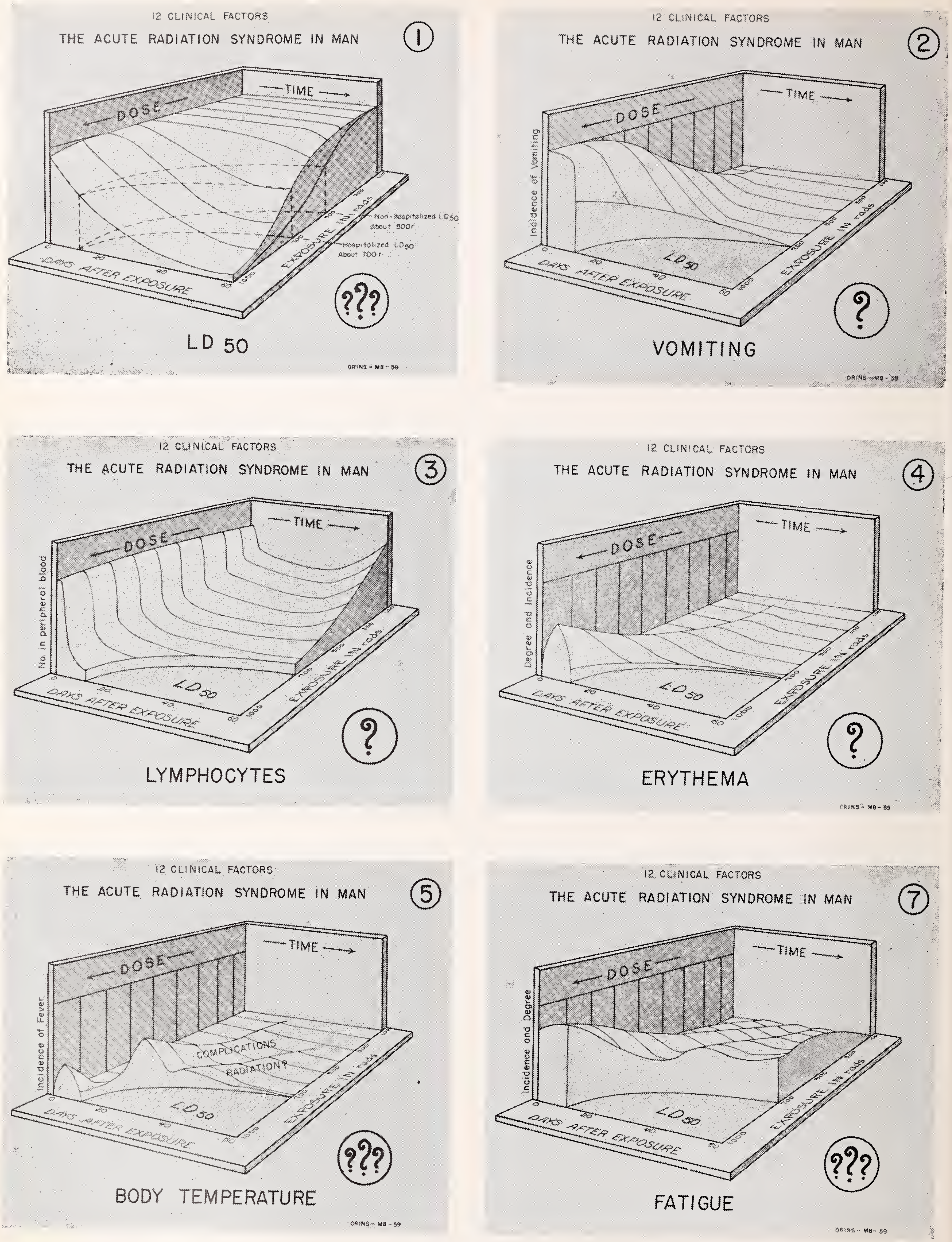
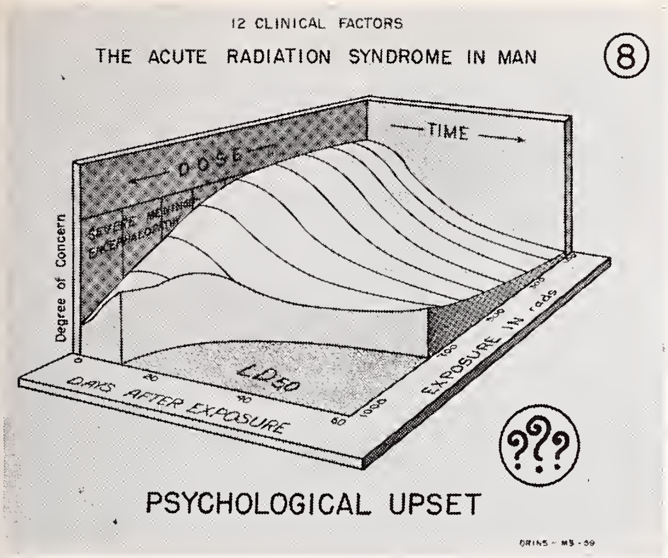
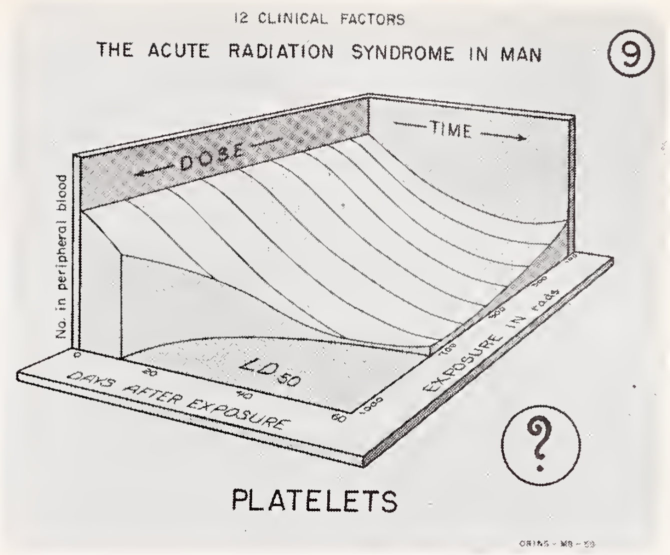
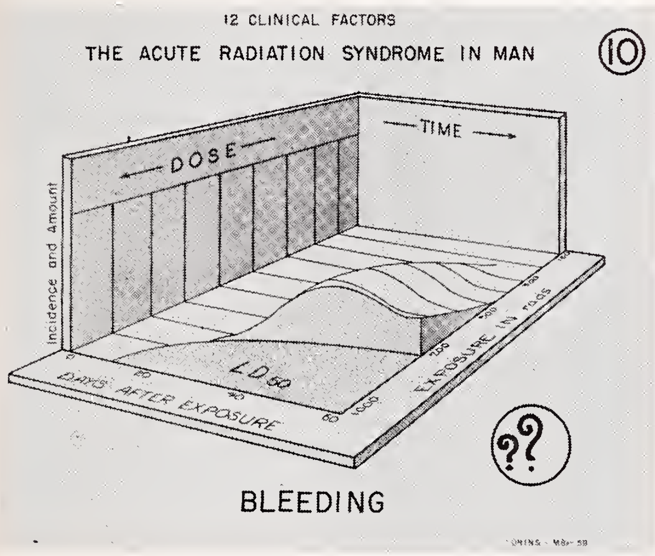
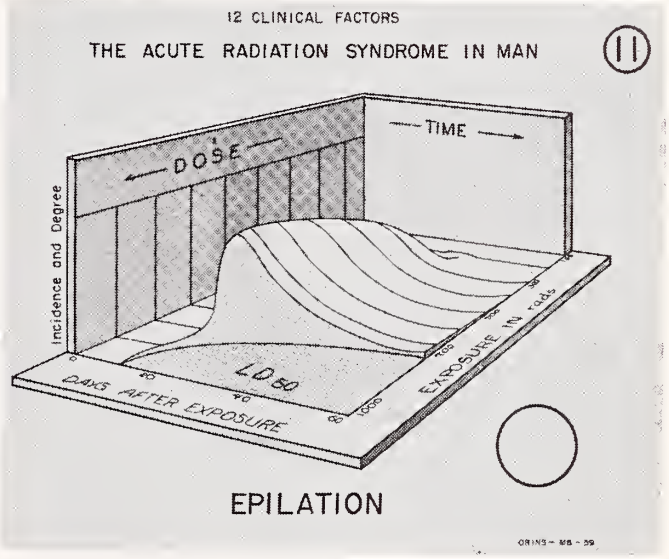


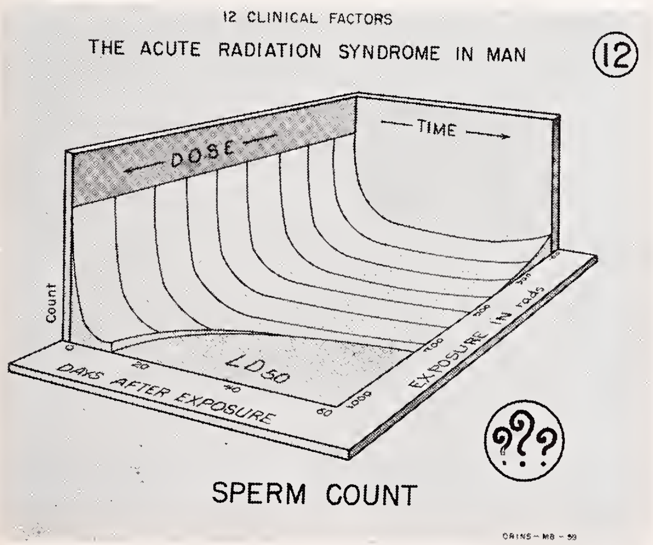
FIGURE III
Eleven features of the acute radiation syndrome and one contamination modification.

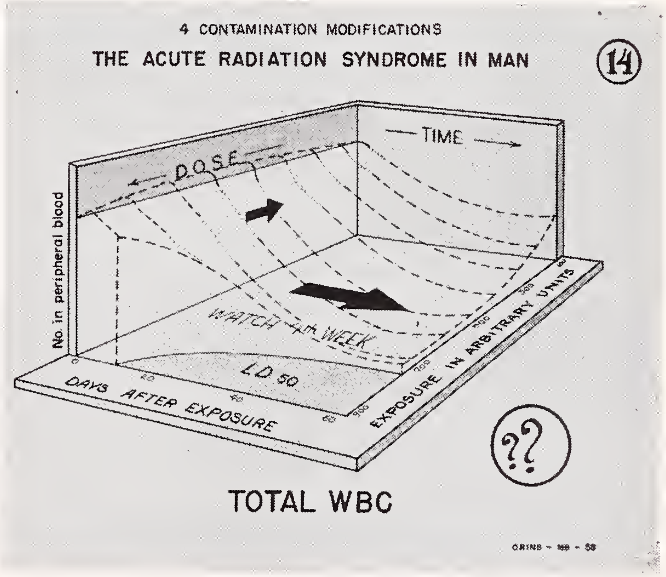

12 CLINICAL FACTORS
THE ACUTE RADIATION SYNDROME IN MAN
⑧
DOSE
TIME
SEVERE MENINGO-ENCEPHALOPATHY
Degree of Concern
0
20
40
60
LD50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN rads
???
PSYCHOLOGICAL UPSET
ORINS - MB - 59


12 CLINICAL FACTORS
THE ACUTE RADIATION SYNDROME IN MAN
⑨
DOSE
TIME
No. in peripheral blood
0
20
40
60
LD50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN rads
?
PLATELETS
ORINS - MB - 59


12 CLINICAL FACTORS
THE ACUTE RADIATION SYNDROME IN MAN
⑩
DOSE
TIME
Incidence and Amount
0
20
40
60
LD50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN rads
??
BLEEDING
ORINS - MB - 59


12 CLINICAL FACTORS
THE ACUTE RADIATION SYNDROME IN MAN
⑪
DOSE
TIME
Incidence and Degree
0
20
40
60
LD50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN rads
EPILATION
ORINS - MB - 59


12 CLINICAL FACTORS
THE ACUTE RADIATION SYNDROME IN MAN
⑫
DOSE
TIME
Count
0
20
40
60
LD50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN rads
???
SPERM COUNT
ORINS - MB - 59


4 CONTAMINATION MODIFICATIONS
THE ACUTE RADIATION SYNDROME IN MAN
⑭
DOSE
TIME
No. in peripheral blood
WATCH 4th WEEK
0
20
40
60
LD 50
DAYS AFTER EXPOSURE
1000
500
300
100
EXPOSURE IN ARBITRARY UNITS
??
TOTAL WBC
ORINS - MB - 59

dip, if it occurs, may take many months. There may be an overshooting above normal levels during the recovery from the second dip. However, this is not indicative of leukemia since the rare cases of leukemia will occur after a few years.

Fatigue (Fig. III, No. 7)

Fatigue might be the most important of all symptoms. Patients who have been exposed to radiation appear to go through waves of fatigue. There are times when they want to get out of bed, and there are other times when they want to get into bed. There is no easy method for measuring this fatigue. The Russians explained it on a purely neurological basis, but at low doses it is difficult to show definite neurological effects. At higher doses, the fatigue presents itself as a definite lethargy. At even higher doses it is a hyperexcitability or even convulsions.

Psychological Upset (Fig. III, No. 8)

Every nuclear accident is immediately followed by "ban-the bomb" demonstrations, sermons on the horrors of nuclear war and newspaper stories about two-headed babies. There are two kinds of psychological upset: first, the upset in the patient himself; second, the disconcerting misinformation attributed to the physician. A most important feature of the psychological upset of the patient is the fact that there is an even greater psychological upset among health physicists and administrators who practice medicine without the responsibility of taking care of patients. During radiation therapy, there is a predetermined dose and highly predictable unknowns in result. In an accident, the dose must be determined after the fact. The result is often indeterminate. Therefore, it is logical to expect arguments on diagnosis and therapy, but these arguments get back to the patient eventually and here they are detrimental to his welfare. The patient usually will believe the worst figures and the worst prognosis. Whether they like it or not, physicians must remember that whatever figure or prognosis is mentioned outloud, it has a legal flavor to it. The legal implications (especially of dosimetry and all the concomitant psychological relationships to patients, friends, and even neighbors) have an importance long after recovery.

The psychological upset that occurs in the patient is usually most prominent soon after the accident and seems to be directly proportional to the lack of real effect. There seems to be a relation to the fatigue the patient experiences. After very high doses the patient does not become fatigued or psychologically upset; he becomes comatose. This might not seem like a clinically important subject, but it probably has more long-term implications than anything the physician will accomplish.

Platelets (Fig. III, No. 9)

After there has been time to get hematological consultation, it is desirable to measure the platelets in the circulating blood. During the first few weeks, the platelet count decreases at any dose. The methods for counting platelets in most hospitals are inadequate at low counts. This becomes a statistical problem at which time it is probably best for the (nonhematological) physician to say "very few," and drop all other numbers.

When the platelet count begins to get very low, it is an indication that bleeding might occur IF it is going to occur at all. In the absence of good hematological facilities, it is probably sufficient to assume that the platelet count is decreasing if the lymphocyte count is decreasing. After a week this is insufficient. After an acute irradiation, bleeding will not occur for a few weeks. During a chronic irradiation, this might not be true. The reason for the platelet count is twofold. First, it might herald the onset of bleeding that would otherwise be unnoticeable; second, one of the methods of therapy might be platelet transfusions. An early platelet count thus becomes a base line for therapy.

Bleeding (Fig. III, No. 10)

Excessive bleeding is treatable; small petechiae are not treatable, but the physician must notice them before the patient. In America especially, all hematological effects of radiation have been emphasized and re-emphasized. A platelet count will indicate whether bleeding might occur, but more than this might be present as a trigger to bleeding. A generation of hematologists believe that bleeding is exceedingly important in the acute radiation syndrome. Neurophysiologists think that it is relatively unimportant. It is probably more highly related to the animals that we must use for investigation than it is to the humans we are trying to treat. Nevertheless, since it is a treatable symptom, it must not be missed by the physician.

Epilation (Fig. III, No. 11)

Epilation is not really a very important medical problem. It might renew a psychological upset in the patient. It certainly will affect the patient's relatives. Patients who have received a large dose of radiation will lose some hair. In the dose ranges of a few hundred rads to the skin, they lose their hair on about the nineteenth day. Since this range of radiation was, at one time, a method of therapy and is still acceptable to many physicians, we have lots of information concerning epilation. In every case, the hair has regrown after a few months. It is a temporary symptom. Its real importance lies in the fact that the physician may increase his stature by predicting its occurrence.

Sperm Counts (Fig. III, No. 12)

We know very little about the sperm count in the human. Apparently it decreases rapidly (days) and stays down for a reasonably long time (months). This means that the person who is irradiated is going to become sterile. Apparently, this is always temporary. The reasons for the "sperm count" becoming an important question to the physician is that when you talk about sterility to a patient's wife or to his family or to his friends or to the newspapers, no matter what words you use, they are not talking about "sterility," but are talking about "impotency." We have no evidence that radiation exposure causes impotency in a patient. One observation indicated that the boar will mount the sow a little less frequently after a high dose of radiation, but we have no evidence of impotency in a human patient. It is surprising how much time a physician will spend in talking to the patient and all his friends concerning this problem of sterility and impotency. It is surprising how many persons are interested in a sperm count. It is also surprising how difficult it is for a physician to get a sperm count.

Chronicity And Contamination Modification (Fig. III, No. 14)

Differing from the acute are the chronic radiation chronic syndrome and the acute radiation chronic syndrome and the chronic radiation acute

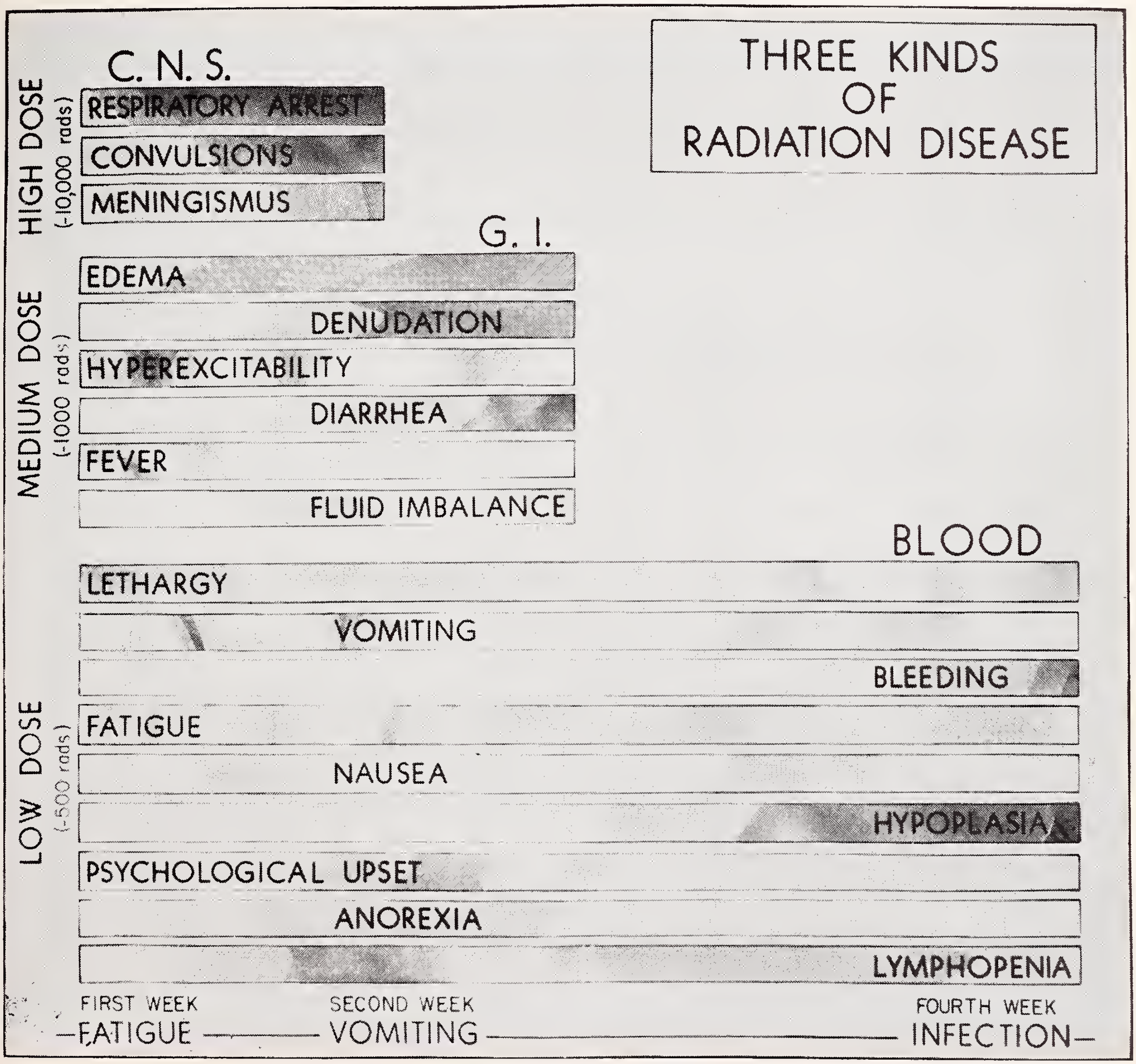


Figure IV
Three kinds of radiation disease.

syndrome. Even if we knew the pattern it would be hard to describe, because the variation in parameters is wide. There have been few accidents recognized, none with measurements proper to a clinical description. From the few observations that have been made and a tremendous amount of animal work, it appears that our guesses might be fairly good. For example, if we accept the total white cell count smoothed out to show a general decrease with time after the exposure, and an increasing effect with increasing dose, then it appears that the chronic picture will be one of a decreased dose. But this is only a decrease in the number of physical units. If we were to accept a biological unit, then the doses would be identical. However, this is largely a matter of semantics. There also appears to be a stretching out of the time span over which the effect takes place. What takes place in a week after an acute exposure might take a month after the beginning of a chronic exposure. Again this is largely a matter of semantics.

Three Kinds Of Radiation Disease (Fig. IV)

In the mouse there are what Henry Quastler[3] has called *modes of radiation death*. The "clinical" pattern that some strains of animals follow is different from that followed in other strains. In the human, there also appear to be distinct modes of radiation death, which manifest themselves as three different kinds of radiation disease. These are all the same disease, and yet the variation in intensity and rapidity of development make the one disease appear to be three (or four, or five, it depends on how precise you want to be).

CENTRAL NERVOUS SYSTEM TYPE

At very high doses, death occurs early, within the first days or even within a matter of hours. There is a clinical pattern similar to a meningitis, but without the infection. At even higher doses, this might be hidden by true convulsions. At even higher doses there might be a sudden respiratory arrest. Such an almost pure central-nervous-system

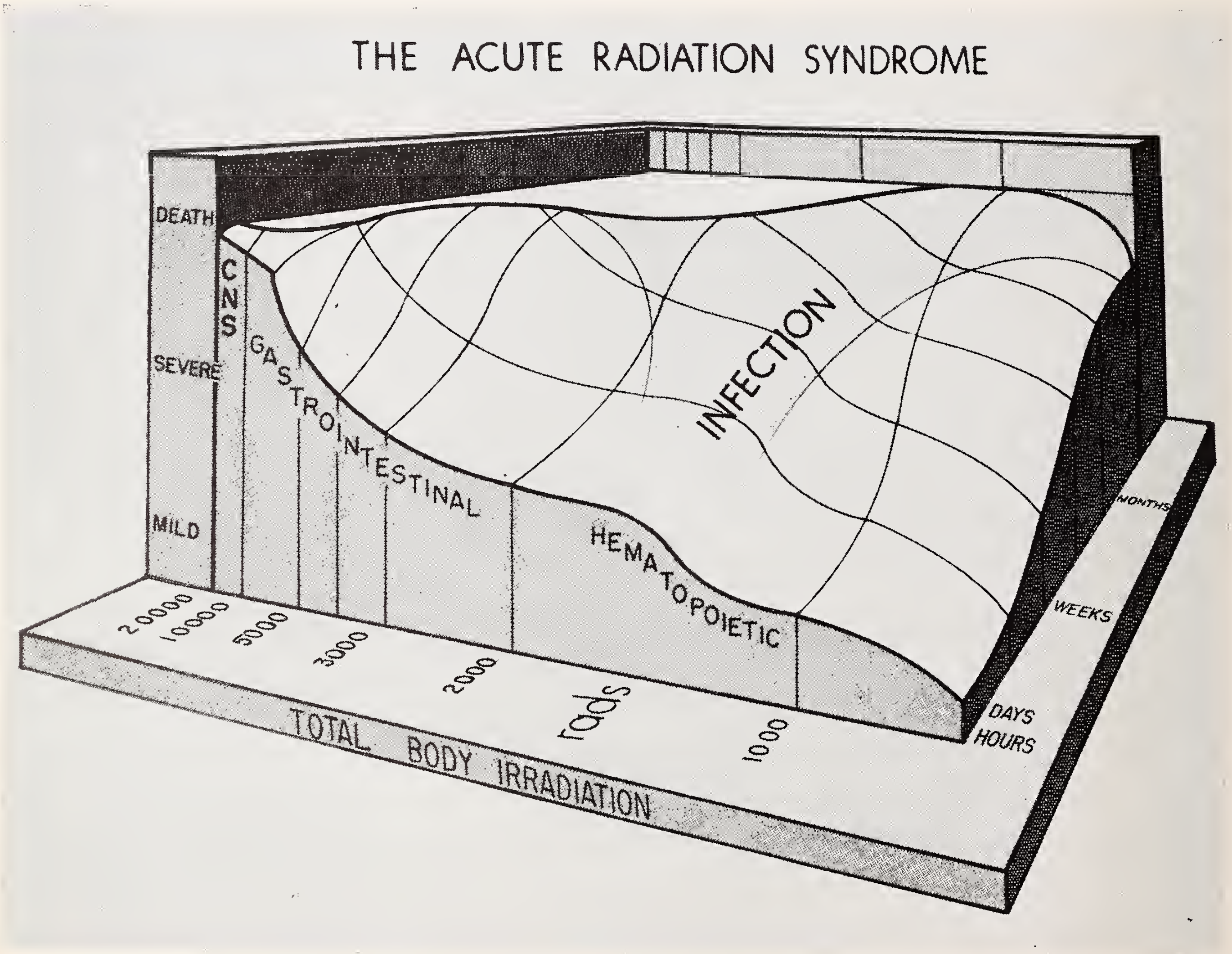


Figure V
A generalized pattern of biological effect.

death has been observed in monkeys irradiated with enormous doses. There probably would be all the other effects, but the patient doesn't live long enough.

GASTROINTESTINAL TYPE

At a lower dose, these central nervous system effects probably also occur, but are not severe enough to cause death. Fever, hyperexcitability and development of a true radiation edema in the central nervous system is probably a less intense manifestation of the same syndrome that at a higher dose caused a quick central-nervous-system radiation death. The animal develops a fluid imbalance. There is a diarrhea, which is probable cause of a fluid imbalance. At higher levels of dose there is probably an actual denudation of the gastrointestinal tract. The animal dies during the second week, or even later. There probably will be vomiting and nausea and anorexia, but these might be hidden by the more severe gastrointestinal manifestations of the disease. The death is gastrointestinal in appearance. The central nervous system effects are not "lesser effects," but they are overshadowed by the clinically more obvious gastrointestinal effects.

HEMATOLOGICAL TYPE

At a much lower dose there is leukopenia, a hypoplasia of bone marrow and bleeding. This usually manifests itself during the third or fourth week. At higher levels of dose the leukopenia would occur but it is overshadowed by earlier convulsions. The hypoplasia certainly occurs at medium dose, but it is overshadowed by diarrhea. If the patient has not received sufficient radiation to kill him in the second week, he will live long enough that severe bleeding becomes the item of greatest concern during the fourth or fifth week.

Infection (Fig. V)

If a person receives less than a thousand rads (this is a highly arbitrary figure) he might die of irradiation, but the death will probably occur after a month or so of disease. If he receives between 1,000 and 2,000 rads he might die within many weeks. If he receives between 2,000 and 10,000 rads, he might die in days to weeks. But, if he receives

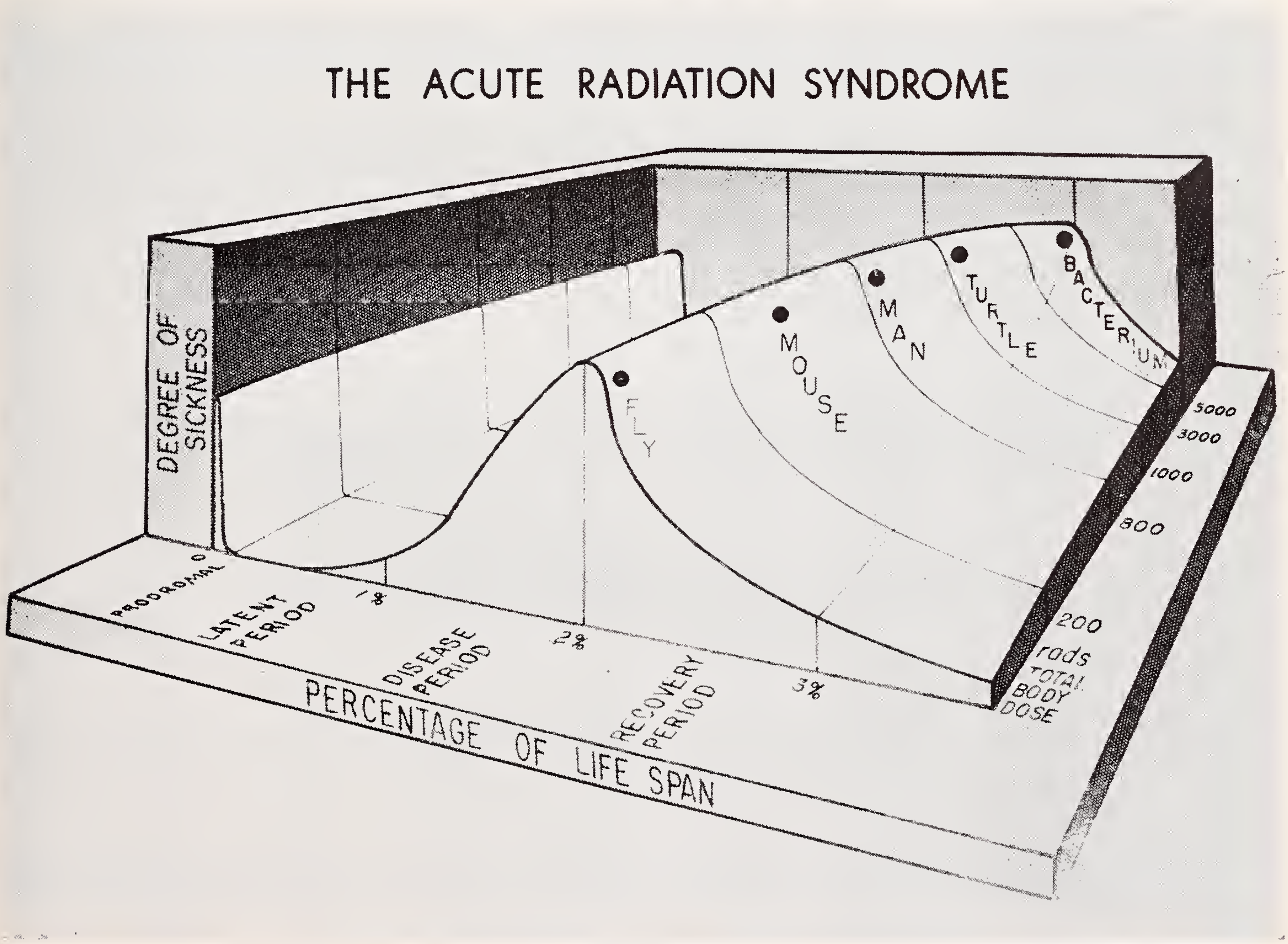


Figure VI
The superimposition of infection on the radiation syndrome.

more than 10,000 rads, death will probably be in less than a day, and the symptoms will be primarily central nervous system.

Spread over this entire range of radiation sickness and death there is one common factor, and this is the probability of infection. Infections usually do not occur in a central nervous system type of death, because the patient dies before infection can develop. It is most common during the hematopoietic portion of the radiation syndrome primarily because these patients do live long enough for infection to develop. And so, over the entire range of acute radiation sickness, there is a possibility of infection. Infection is not a part of the radiation itself, and its occurrence within the hematopoiectic portion of the syndrome is probably not really hematopoietic any more than it is really radiation induced, but we choose to place it within this classification because it has a purely temporal simultaneity and except to an expert hematologist or immunologist it is probably the same portion of the body that is being affected.

Biological Identity And Difference (Fig. VI)

All animals probably go through the same general pattern of disease after an acute radiation exposure. If, instead of using chronologic time, we use the lifespan as the biologic unit of time (and do not argue about what we mean by lifespan) then a fly, a man, and a bacterium all live to 100% of their lifespan. When given a just sublethal dose of radiation for this particular animal, all of them go through a very rapid prodromal period, after which there is a seeming recovery. Within about one per cent of the animal's lifespan, there is a latent period. This is short for a bacterium; it is also short for a fly, but it is about the same relative fraction of its lifespan. Following the prodromal period there is a latent period during which the animal appears to be perfectly healthy. The healthy appearance is probably true only symptomatically. It is remarkable that in animals that hibernate naturally, if they are put into hibernation during the latent period, the progression of the radiation disease is also hibernated, but resumes at exactly the same point when the animal is brought out of hibernation.

The length of the latent period might be slightly modified by treatment; it is certainly highly modified by dose, by dose rate and probably by all of the other characteristics of the disease.

The disease period follows a latent period and seems to last another per cent of the animal's lifespan. Then, there follows a recovery period that also last about one per cent of the animal's lifespan. However, this is highly modifiable by our definitions of what we mean by recovery. The recovery from a psychological upset in a human might take much longer than one per cent of the lifespan. The same kind of effect is not even considered in a bacterium. Such a generalization, that all animals go through the same pattern of disease, is useful because much of the study cannot be done in humans and must be done in animals. The generalization is useless if it should attempt to relate sperm production in a human with a nonsexual reproduction in a bacterium. Radiobiology in animals is extremely valuable, but it is not the practice of medicine. Although it has been exceedingly difficult to include in the crowded educational curriculum of health physicists and administrators (and is probably impossible in newspapermen) it should not be difficult for physicians to understand that mice are different from men.

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1. Benjamin, E., von Reuss, A., Sluka, E., Schwarz, G., Wein. klin. Woch. XIX (26), 1906.

2. Shipman, T., Unpublished Talks, Summarized in J. Occ. Med. 3 (3): Special Suppl., March 1961.

3. Quastler, H., Fed. Proc., 10: 106, 1951.

Science And Humility

The truly scientific spirit, then, should make us modest and kindly. We really know very little, and we are all fallible when facing the immense difficulties presented by investigation of natural phenomena.—Claude Bernard, M.D. *An Introduction to the Study of Experimental Medicine.* New York, The Macmillan Company, 1927, p. 39.

III. Short-Term And Long-Term Effects

A. Some Aspects Of Basic Radiation Biochemistry*

Hiroyuki Hatano, Kyoto, Japan†

■ We don't know exactly how ionizing radiations affect biochemical reactions, but we do have some of the basic facts. There is ionization and excitation of the molecules participating in the absorption and transfer of the kinetic energy of radiation probably during about 10^{-15} to 10^{-5} sec. Many mutations and somatic changes can be detected only after a few full days or even after several years. Doses in the order of a few milliroentgens to a few hundred roentgens may produce noticeable effects in living cells; contrary to this, doses of several million roentgens are necessary to cause ordinary chemical reactions observable in chemical systems. Thus, it appears that there is a discrepancy between radiobiological phenomena and radiation chemical reactions.

However, it is believed that many successive chemical reactions might happen in one local area. These reactions might range from purely physical processes to distinct biological phenomena. The biochemical processes may ultimately be conceived in terms of purely chemical reactions, but are somewhat obscure because they range between the fields of physics and biology. This field of radiation research is called "radiation biochemistry."[1]

The general scope of radiation, its wide range in chronologic time, the kind of change that takes place and the biologic effect are indicated in Table I. The feeling that this must all be a part of a unified radiation—effects theory combined with the progress of molecular biology during the past few years has excited studies in radiation biochemistry.

Direct Action

Since the beginning of radiation research, two controversial mechanisms have been proposed: a *direct action* and an *indirect action*. The indirect actions are favored by chemists, but the chemical mechanisms of a necessary direct action have had less emphasis. Recently, electron spin resonance spectroscopy, gas and liquid-chromatography and other experimental methods and theoretical treatments have become possible. These are just now beginning to give evidence on the direct mechanism.

During the initial process, under anaerobic and anhydrous conditions, some electrons are ejected from their parent atoms to produce unpaired electrons. These electrons may now be detected by electron spin resonance spectroscopy. Many kinds of free radicals with unpaired electrons appear after irradiation. Free radicals have been produced from irradiated molecules of amino acids,[23] peptides,[4] proteins,[25] carbohydrates,[67] steroids,[8] vitamins,[8, 9, 10] nucleic acids,[11] enzymes, [5, 12] coenzymes,[9] and also from cellular particles.[13] Even tissues are more chemically reactive after irradiation and there may be recombinations.

When a recombination occurs between fragments of the same molecule, a *dimer* of the molecule is produced. Successive reactions may give polymerization. The products of a reaction, however, may combine with other free radicals or even with other molecules. These may produce still other radicals or molecules, which may or may not

TABLE I

SCOPE OF RADIATION BIOCHEMISTRY AND ITS RELATION TO OTHER RADIATION RESEARCH

SCIENCE	IRRADIATED OBJECT	CHANGE	TIME OF RESPONSE
Radiation Biology	Multicellular organism	Death	day-century
		Somatic	" "
		Visible	hr-year
	Cellular system (Bacteria, Yeast, Virus)	Microscopic	min-hr
		Mutation	min-hr
		Physiological	min-hr
Radiation Biochemistry	Subcellular particle (Nucleus, Mitochondria Microsome) Biochemical system (Metabolism, Multienzyme system)	Biochemical (Direct or Indirect)	sec-hr
Radiation Chemistry	Macromolecule, (Small molecule, or Atom)	Molecular (Radiolytic, Synthetic)	10^{-5} sec
Radiation Physics	Subatomic entity	Primary lesion (Ionized, Excited)	10^{-15} sec

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* *This article has been rewritten by Marshall Brucer from the author's original document. Mistakes in interpretation of the chemical language should not be attributed to the author, but to the rewriter.*

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be reactive and may or may not produce still further reactions. A schematic presentation is

$$A, B, \ldots \rightarrow A^{\cdot}, B^{\cdot}, \ldots + n\,e$$
$$A^{\cdot} + A^{\cdot} \rightarrow AA$$
$$A^{\cdot} + A \rightarrow AB^{\cdot}$$
$$A^{\cdot} + B^{\cdot} \rightarrow AB$$

Radiation-induced electron vacancies on any area of the surface of a large molecule (proteins, nucleic acids) appear to be capable of migration to another place on the molecule. Apparently, electron vacancies may even transfer beyond the initial molecule through linkages between molecules.

Substances already biologically active (enzymes and coenzymes) are inactivated by gamma-irradiation even though free radicals may be produced from the irradiated substances. This is a kind of radiation damage. If the *radiation* damage is in the *active center* of an enzyme the inactivation may occur as soon as there is a change in the conformation of the molecule. Where the damage is not in the active area, the destroyed electronic structure may have to be transferred to the active area before there is inactivation.[12] This may be an explanation of a short delay of apparent chemical reaction.

In living cells or in complex mixtures of reactive chemicals and with many individual molecules, radiation absorptions may occur. It has been proposed[14] that the proper combination of such events may be the ultimate cause of mutations and carcinogenic changes in tissues. Whether or not the basic chemistry is exactly as stated, it is sufficient to realize that there is the possibility of a logical and demonstrable explanation.

Indirect Action

The mechanism of indirect action is relatively well established. It is generally agreed that the solute molecules react with the radiation products of water. Such radiation products as OH, H, O_2H and H_2O_2, give oxidation or reduction products of the solute.[15] There are a number of examples that support the validity of this mechanism. The chemical methods have to be sensitive enough to detect somewhat esoteric changes in the properties of biochemical systems. Observations have been reported on the inactivation of some enzymes[16, 17] and on a change of the spectropic behavior of some coenzymes.[9] These result from even moderate doses of X- and gamma-irradiation in aqueous solutions.

It has been well established that sulfhydryl enzymes are inactivated reversibly by moderate doses of irradiation through an indirect mechanism:[18-21]

Inactivation:

$$2\,ESH + 2\,OH \rightarrow ES-SE + 2\,H_2O$$
$$2\,ESH + O_2H \rightarrow ES-SE + H_2O_2$$
$$2\,ESH + H_2O_2 \rightarrow ES-SE + H_2O$$

Reactivation:

$$ES-SE + 2\,RSH ---- 2\,ESH + RS-SR$$

Definitions:

ESH = active sulfhydryl enzyme
ES – SE = inactive enzymes
RSH and RS — SR = reduced and oxidized thiol compounds (such as cystein and glutathione).

Heavily irradiated enzymes are inactivated irreversibly. They may be completely decomposed. Amino acids may be deaminated and decarboxylated in irradiated aqueous solution. The radiosensitivity of amino acids can hardly be the same even though they may be similar in chemical structure.[22] Deamination has been demonstrated to proceed oxidatively through intermediary carbonyl compounds such as keto acids:[23]

$$H_2NRCHCOOH + OH \rightarrow H_2NRCCOOH + H_2O$$
$$H_2NRCCOOH + O_2H \rightarrow HN = CRCOOH + H_2O_2$$
$$HN = CRCOOH + H_2O \rightarrow NH_3 + RCOCOOH$$

The keto acids are the least stable in aqueous solutions and hence are decarboxylated successively to result in aldehydes as follows:

$$RCOCOOH \rightarrow RCHO + CO_2$$

A peptide bond may be cleaved oxidatively to produce fragmental carbonyl compounds. This may occur together with hydrolytic cleavage of the bond, which may be further deaminated and decarboxylated successively:[24]

$$H_2NRCHCO-NHR'CHCOOH \rightarrow + NH_3 + R'COCOOH$$
$$H_2NRCHCO-NHR'CHCOOH \rightarrow H_2NRCHCOOH + H_2NR'CHCOOH$$

Proteins, in aqueous solutions, may be decomposed according to the schematic mechanism shown in Fig. I. The radiosensitivities of the constituent amino acids of proteins may be different from the

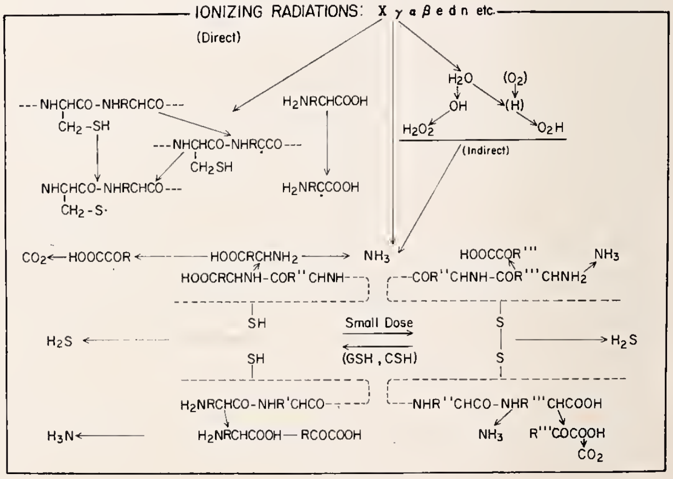

Figure I

Schematic mechanism of radiation change in one biochemical compound.

radiosensitivities of free amno acids in similar aqueous solutions.[22] Following this same (Fig. I) schematic presentation, nucleic acids,[26] carbohydrates,[27] steroids,[28] vitamins,[29] hormones[28] and other compounds may be brought to radiolysis indirectly by the radiation products of water through successive secondary reactions.

Effect Of Biochemical Systems

One of the important differences between the radiation effects on a biochemical compound and on a whole biochemical system is that the inactivation of the *total biological activity* does not appear always to be additive. For example, alcohol dehydrogenase needs a coenzyme, diphosphopyridine nucleotide, for the appearance of its full activity. Moderate doses of gamma-irradiation are more effective when the holoenzyme is irradiated than when the apoenzyme and coenzyme are irradiated separately.[30]

The effects of irradiation of enzymes and enzyme systems localized in subcellular particles (mitochondria, microsomes, nuclei) have been investigated *in vitro*. The activities of some of the enzyme systems in nuclei appear to be relatively more radiosensitive than the same systems in mitochondria.[31] Thus it appears, in general, that ionizing radiation may cause biochemical damage to the dynamic equilibrium of living systems along with chemical damage to the biochemical constituents of the same systems. The damage can be observed when the chemical methods are sufficiently sensitive to detection. It is believed that there are no different events in chemistry *in vivo* than those observed in chemistry *in vitro*.

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Student Days Of William Harvey At Padua

Harvey, who proved to be Fabricius' hardest-working student, became the spokesman of the small group of Englishmen and was elected their representative. Each nationality had such deputies, and every two years they participated in the election of the new rector. They would also hold conferences during which they often rose up to rail vociferously against the professors. The students at the law college also elected Harvey to be their representative, which was no small matter, since in the life of the University the law students were considered much more distinguished than the medical students and accordingly enjoyed more authority.

Harvey entered Fabricius' institute which was then in the midst of the most intensive research and discussion. Fabricius had just collected the material for his book on the development of animals, after which he intended to summarize his findings on veinous valves. Such ventures involve a tremendous amount of reading, dissecting, thinking, and the young medical student entering this whirlpool of scientific problems naturally tends to absorb an abundance of enthusiasm and assurance at being considered worthy to participate in such important matters. Harvey, who was small compared to his strapping compatriots, with black wavy hair, and who spoke with lively gestures in a manner more Italian than English, threw himself passionately into the problems of the development of the embryo and the movement of the blood.—Tibor Doby, M.D. *Discoverers of Blood Circulation· From Aristotle to the Times of Da Vinci and Harvey.* New York, Abelard-Schuman, 1963, p. 187.

III. Short-Term And Long-Term Effects

B. The Long Time Effects Of Nuclear War

R. R. Newell, M.D.

■ The most important long time effect of a nuclear war will be the enduring disruption of social organization. The death of large numbers of "key personnel" itself will cause the destruction of the machinery of our culture. Our civilization is complex and its elements interdependent. You are as well equipped as I to predict the effect of the devastation and to prophesy how long to rebuild our way of life. I'm going to limit myself to the long time effects of irradiation. Next after the magnitude of its capability for destruction, nuclear bombing is characterized by the amount of radiation it produces and the radioactivity it leaves behind.

The persons killed by the immediate radiation, thermal or nuclear, are properly accounted battle casualties and so are those caught in the subsequent radioactivity. We call them "killed in the bombing" even though they may walk around for days or weeks before death overtakes them. About two per cent of those so heavily irradiated that they barely recover from the acute effects will die of leukemia sometime between one and fifteen years later. I would like to class these as battle casualties, too. This means that when you count casualties after battle, instead of reporting 50 per cent dead, you report 51 per cent killed. To be sure, you can get some work out of the one per cent before they sicken, but so can you get some work out of the more heavily irradiated between the time of the prodromal symptoms and the onset of the fatal radiation sickness.

There will be large areas of a thoroughly bombed country in which radioactivity is down to a quite tolerable level by the time people come out of their shelters. Shafer[1] made an estimate for the Congressional Hearings of June 1957. He assumed about 2500 megatons of nuclear bombing distributed over the United States. After two weeks, 85 per cent of land area would have a residual exposure rate below 0.1 r/hr.

Machta[2] estimated the worldwide fallout based on 4000 megatons world total nuclear bombing (half fission, half fusion). Fifty million curies of Sr^{90} would be available for worldwide fallout, in addition to what is in local fallout. He arrived at an average of about 1000 millicuries of Sr^{90} per square mile, some 20 times the level produced by bomb testing up to that time. One will have to expect a much larger amount of bombing in any actual nuclear war. A large amount of C^{14} will be produced, too; Dr. Machta calculated that it would reach a maximum about 20 times natural background and then gradually diminish as it gets redistributed (mostly into the ocean).

The enduring hazards to health from the radioactivity will be mostly from the long-lived nuclides, Sr^{90}, Cs^{137} and C^{14}. (During the actual fallout, the external irradiation is most important.) At Rongelap Island,[3] the natives received about 175 r from the local fallout, yet the amount inhaled and ingested gave them a negligible body burden of radioactivity. In 1954, the year of the fallout, estimated body burdens in the Rongelap people exposed were 2.7 microcuries of Ba^{140}, 1.6 microcuries of Sr^{90}, 1.2 microcuries of rare earths and 6.4 microcuries of I^{131}. The latter appears large, but it is in the low range of diagnostic medical dosage. The amounts of Cs^{137} and Zn^{65} seven years after the fallout are insignificant because of the biological turnover in the interval. From a large pooled urine sample, the average Sr^{90} body burden was calculated to be 6.9 millimicrocuries.

The Late Sequelae

The commonly recognized late sequelae of irradiation are leukemia, cancer, shortening of life-span and genetic mutations. Cataract is not worth taking the time to discuss (say I).

Leukemia

Radiation is leukemogenic. This is easily proved in experimental animals and has been observed among survivors of the Hiroshima and Nagasaki bombings. Good quantitative analysis is available from the medical histories of 11,000 men in England that received X-ray treatment for spinal arthritis.[4] The leukemia induced was mostly of the acute type, some chronic myelogenous, and little chronic lymphatic. In England nearly all appeared between one and six years after irradiation; in Japan the effect developed more slowly and lasted longer. I think we can say with some confidence: an integral dose of 100 rads (total-body) will double the natural likelihood of getting leukemia (fifty per million per year). A total-body exposure so large

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that one barely recovers from the acute effects will give a two per cent probability of leukemia sometime in the next 15 years.

Scientists do not agree on the extrapolation of these observations to predict the effect of small doses. Take 100,000,000 persons unirradiated. One expects 50,000 leukemia cases in 10 years. Now suppose this entire population exposed to one roentgen (0.5 rad total-body dose). Some analysts would say that this is below the threshold of effectiveness and no extra cases of leukemia are to be expected. But if one denies the threshold and assumes a linear relationship, one expects to see in the next ten years, not 50,000 cases but 50,250 cases. Some essayists (I'm one) think that a quadratic rule fits the data far better. On this basis the 1 r exposure of 100,000,000 persons would produce two or three extra cases, an increase of less than 0.01 per cent of natural leukemia incidence.

Cancer

The carcinogenic action of radiation has been long known and much investigated. Much of the human data concerns therapeutic irradiation applied to very limited portions of the body.

Clinical radiologists form the only large group subjected to total-body irradiations, but the doses are not known. Although many of the X-ray pioneers died of cancer, yet most cancers were epidermal and not pertinent to our discussion of penetrating gamma rays.

Among the Hiroshima and Nagasaki survivors, some carcinogenesis has become evident, but with a long latent period compared to leukemia. It may, in the end, add up to a larger total than the leukemia.

Shortening Of The Lifespan

Although radiologists are not notably short-lived, yet oft-quoted speculative prediction is this: on the average, a total-body exposure to 1 roentgen shortens life 10 days. Nobody has taken a thousand men at random, given each 100 r and followed their lives to the end to see if they fall an average 1000 days short of life expectancy. So, we don't know. Unless somebody does such an experiment with 5 r to a million men, we'll never know. In fact, it would take a good many million men to prove the effect of 1 r.

We lack data on human exposure of the whole body. Partial-body irradiations are less injurious even when the local dose is augmented to make the total energy absorption the same. Clinical therapy does provide some evidence. I followed the lives of 200 women cured of cancer of the uterine cervix by irradiation. The integral doses were comparable to a total-body dose of 30 to 170 rads in a 70 kilogram man. Followed for 10 to 30 years after irradiation, this group of women matched the standard life table almost exactly. That is to say, no effect on longevity was observed. We can only suppose that the life-shortening of persons moderately irradiated during and after a nuclear war will have little effect on life insurance premiums.

Genetic Effects

The heredity of the human race is imbedded in 23 pairs of chromosomes, each set with a large number of genes. The genes are presumed to be large organic molecules (molecular weight a million or so). Watson and Crick have received the Nobel Prize for their "zipper" model of the gene, accounting for specificity and self-replication. We can suppose that each gene is unique—no other identical molecule in the cell. A change in the gene makes a unique change in the cell and in all its progeny.

This uniqueness of the gene is important in our concept of radiation injury. We know for sure how radiant energy is absorbed in matter—it's absorbed in little pieces, not continuously. A gamma ray may pass through a cell with no effect at all. The cell is so small and thin that it has little chance of stopping a given gamma ray. If some atom in the cell does trip up the gamma ray, the gamma ray kicks an electron out at high speed and goes on with energy that is much diminished. The high-speed electron, passing other atoms, pushes other electrons out of their structure, producing charged ions. If the gamma ray gives a lot of energy to the high-speed electron, the latter will make thousands of pairs of ions before it runs down. Each act of ionization, of course, disrupts the molecule that the ionized atom happens to be in.

The path of ionization courses in a crooked manner through several cells, perhaps, leaving a swath of broken molecules. The fragments are chemically active and do lots of things to the structure of the cell. When a "living" molecule is ionized the effect may be chemically specific. If it is a gene molecule, the specific change may alter its function radically. If the gene is in an ovum or sperm that goes to form a fertilized egg, the molecular injury caused by the radiation may make itself evident in an alteration of a heritable character. If so, we call the effect a mutation.

I have risked being tedious in this step-by-step recounting of radiation-induced mutation because on this picture rests our solid conviction that even the least irradiation (even one gamma ray) has a finite chance of producing a mutation. That is why scientists say with confidence; *"There is no radiation dose so small that it is without biologic effect."* This is popularly translated, *"Even a little radiation* *is biologically important.*" The apparent truth of this depends upon what you mean by "important."

Natural Experiments in Mutagenesis

In the State of Kerala in India are some sea beaches containing a lot of monazite sand (an ore of thorium). They are therefore radioactive. The people (fisherfolk) who live on the beaches have been receiving up to 10 or 20 times as much radiation as people who live in villages nearby. A population of 80,000 persons has been so exposed from time immemorial—perhaps 100 generations. The U.N. Committee planning to study these people calculates that it's nip and tuck whether the genetic effect of that much radiation for that many generations will be observable by the demographic techniques today available. Perhaps this is a good place to draw the line:

Irradiations less than one r per year are unimportant.

GENETIC EFFECTS OF LARGER DOSES

Speculative analysis of the genetic hazard would be better if we knew how many genes man has and what the natural mutation rate among them is. Considering how complicated is man's structure and how multifarious his activities and adaptations, we can guess how much we'd have to program into a computor to imitate him. This is what has to be packed into the genes.

Vinegar flies have four pairs of chromosomes; man has 23 pairs. Geneticists have identified and mapped hundreds of genes in the fly. Surely man needs more than a fly does. Perhaps 100,000 genes is not too big a guess for man. Each person has his particular assortment; differing, of course, from the 100,000 that belongs to another person. Many genes, no doubt, are held in common, the same in everybody; but differing from the collection that makes a mouse ovum grow up to be a mouse. There must be a racial inventory of thousands of genes that are held alternatively. Four of these are known to be characteristic for skin color of the Negroes who were brought to the U.S., but only one characterizes the blacks of South Africa. There are any number of bodily traits that reveal the presence of a particular gene in a person's inborn composition.

Hereditary features vary greatly in their importance to health or society. The distinction between a normal variation and a mutation is arbitrary. Color blindness is called a mutation; blue eyes are called normal. The pool of mutant genes that the human race draws from is variously estimated from a few thousand to 8000. Possible (but not lethal) changes in the gene are continually recurring. Those that are vitally or culturally disadvantageous are gradually deleted by selective mortality. The average number of mutations in a population is obviously an equilibrium between mutation and deletion rate.

Every person, no doubt, harbors mutant genes, some dominant, some recessive The average number has been estimated from 1½ to 8. Of the modest number of known mutations in man, a dozen or so have had their frequencies counted. Estimated mutation rates per generation per million persons run from four (albinism in Holland) to more than 10 times that. Muscular dystrophy is said to have a rate of 45 in Ireland, 43 in England and 95 in the U.S.

RECESSIVE MUTATIONS

Most of the load of mutant genes is carried beneath the surface, because many mutations are recessive and are exposed to the force of differential mortality only when chance brings them together from both parents. We suppose that few genes are completely recessive. Even though the constitutional effect may be subliminal, it is presumed by many geneticists that the occurrence of a half dozen recessive mutations is likely to produce a perceptible injury to health.

HOMOZYGOSITY

When we first began to worry about the bad genetic effects of radiation, it was usual to extol the beauties of genetic purity. The ideal was conceived to be a genetic constitution composed entirely of the best genes. Why settle for less? More recently our attention has been called to the racial, and even the individual, advantages of heterozygosity. One doesn't have to subscribe to the popular superstition that the mongrel is tough and the pure blood (homozygous) sickly. One has only to look at organic evolution and see that mutation occurs in only one gene of the pair (paternal-maternal) and that a mutant gene has to be preserved in heterozygous state in order to get a chance to prove itself in competition.

HETEROZYGOSITY

"Hybrid vigor" is known in agriculture and horticulture. It has been attributed to the additional variety of vital reactions brought in bv the nonconforming genes. To this we attribute the 20 per cent increase in yield of commercial hybrid corn. One can cite some examples where the advantage to the heterozygote is definite and specific. The most famous is the high frequency of sickle-cell trait among certain African tribes. You'd think that high mortality would cause the mutation to disappear from the race. It transpires, however, that the malaria parasite find sickled red cells unsuitable. Consequently, the tendency to sickling that occurs in the heterozygote makes him resistant to malaria and gives him an advantage over the pure-blood normals. And so the mutation is preserved in the heterozygote and the homozygotes die off.

COMBINED EFFECTS

Whatever mutations do occur, spontaneously or induced by irradiation or mutogenic chemicals (or whatever), may die out or may proliferate and spread through the population. It has been pointed out that a mutation that does only a little harm is really more damaging than one that does a lot of harm, for the latter will soon be eliminated from the population by differential mortality. It will be many generations before the *slightly harmful gene* falls into a gentic complex where its effects are critical and lead to death or sterility. This aspect of the matter can be put very pointedly thus: every mutation put into the race requires an early death in some future generation to get it out again. I heve even told my fellow radiologists: *"The doubling dose of radiation is 50 r. Keep a record of the pelvic irradiation to your young women patients even though it's only a fraction of a roentgen each. When the sum of all the ovarian radiation reaches 50 r, cut a notch in the switch handle of your machine, for you've killed a man. You don't know how many generations away it will be and you'd never be able to identify him nor could he identify you. But in some one of those women probably occurred a mutation that will stay in the race until death takes it out."* I no longer feel badly about it. It is impossible to say whether an increase in the mutation rate with consequent increase in variability of the human race is bad for mankind, or good.

Evolution

I could even put my tongue in my cheek and argue this way: mankind has got himself into a deadly fix. He has conquered the problems posed by Nature one after another until he could now live in safety and in plenty. But the problems posed by mankind and his truculent nature (with a small n) he has not solved. Organic evolution is a genetic adaptation to Nature and has gone most rapidly in past ages when the environment was changing most rapidly. *"Evolution occurs in times of stress."* But today man is changing his own environment at such a rapid rate that the slow Darwinian process (survival of the fittest) is totally unable to keep up with it. Maybe more mutations would be the saving of the race, even though many mutant men may have to die for it. The price of evolution, of course, has always been mortality.

I'll now remove my tongue from my cheek and say: obviously genetic evolution is too slow to save us. We shall have to depend on social (cultural) evolution.

Over-all Genetic Effect

Neel[5] has said how misleading it can be to quote actual numbers in this matter where we have so little dependable quantitative information. We do have the Russells' report on some half million mice. It was their work that showed mammalian susceptibility to be 10 to 15 times greater than that of the fruit fly, on which we'd been basing our earlier estimates. Neel let himself be persuaded to make quantitative estimates. He used Russells' figure for radiation mutagenesis—1 to 4 ten millionths per gene per roentgen of exposure. He assumed 40,000,000 persons surviving having suffered a total gonodal exposure of 300 r to 600 r. He inferred at least 24 million mutant genes to be handed on to the next generation, but not more than 970 million. Many would result in intrauterine or early childhood death. One per cent to four per cent, he said, would mean marked abnormality or severe handicap. Some 50 per cent or more would not be incompatible with life but would be such as could contribute to loss of vigor and fertility, and subtle effects that shorten the average lifetime somewhat.

The genetic effects would be distributed through some 30 generations. Some six per cent might even appear in the first generation. Thereafter, they'd be a bit less frequent but probably increase again after a number of generations. Neel estimated the total number of 30 generations—0.3 million to 38 million obviously defective persons, 5 million to 384 million fetal or perinatal deaths, and 12 million to 768 million with impaired vitality. Such large numbers can easily be meaningless or misleading. A better way to state the same estimates would be as a fraction of the numbers expected from the mutations that occur naturally. About four per cent of babies born have some congenital defect (more than a "stork bite" on the nap of the neck). Half of these (two per cent of babies) are hereditary genetic effects. In the 30 generations after heavy nuclear bombing, somewhere between one per cent and 61 per cent of all the congenital defects would be attributable to the bombing, the rest being just those normally expected.

It was Neel's belief that the human race could survive and recover from such a sublethal general irradiation—once.

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William Withering

Withering's first use of foxglove in his practice was in 1775, the year before he left Stafford for Birmingham. How it was first called to his attention is of such interest that it is given here in his own words:

"In the year 1775 my opinion was asked concerning a family recipe for the cure of dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed. I was informed also that the effects produced were violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in these subjects to perceive that the active herb could be no other than foxglove."

The knowledge of the use of foxglove in dropsy may have been known in household medicine in that part of England just as a knowledge that cowpox protected against smallpox was known in Gloucestershire long before the time of Jenner. It needed a man like Withering to study in a scientific manner the effects of this rural remedy and introduce it to the pharmacopeia just as Jenner had taken the countryside tradition of cowpox and by study and observation developed the practice of smallpox vaccination from it.—Louis H. Roddis, M.D. *William Withering: The Introduction of Digitalis Into Medical Practice.* New York, Paul B. Hoeber, Inc., 1936, p. 50-51.

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THE PRESIDENT'S PAGE

One of these days, American physicians will have to face up to the question of what kind of medical practice shall prevail in our nation. Shall it be free enterprise, private practice or government controlled practice? That there will be modifications imposed by more and new forms of 3rd party payment appears to be inevitable. But who shall dictate the terms of these requirements—the third parties involved, or the medical profession? No one will deny that there must be change, but who shall direct the changes and to what extent? Shall it be Blue Shield which establishes physicians fees—shall it be insurance companies? Shall these fees be at "wholesale" rates rather than at customary professional levels and what percentage of the population shall be served by the profession at these "wholesale" fees?

Unfortunately, this isn't a job for just the few physicians who interest themselves in medical society activities. If every physician in the country were to interest himself as fully as the few, we would still represent a minority interest in the affairs of the nation. The difficulty is that we have the choice of being a potent minority, with an influence commensurate with the high degree of skills represented by our professional attainments—or an impotent minority a condition imposed upon us by the broad-based disinterest so patently evidenced by some 90 per cent of our colleagues.

Perhaps politics is a dirty word to many of us, although it can have a higher conotation. For many years we have, as professional people, disdained politics. Today, however, we are up to our eye-brows in politics on a national level, and not a form of politics which we evolved for the attainment of our aims, but a politics imposed on us from without, and which places us on the position of appearing to be against everything; against the sick, against the aged, against a benevolent paternalism which is only humanely interested in alleviating the distress of a long suffering public. Frankly, its a frustrating experience, and I wouldn't mind if more of our colleagues became more keenly aware of this frustration. But its more than just frustration. It's dangerous to our profession, and to the welfare of our country.

Did you suppose that the new administration would allow medicare to die of inattention? Well you know better now. In his "State of the Union" address on January 8, Medicare stood high on President Johnson's legislative program—after Civil Rights, tax cuts, and unemployment. In New York State, both Senators Javits and Keating favor their own compromise version of the King-Anderson Bill, and have the staunch support of such other Republican Senators as Kuechel (California), Cooper (Kentucky), Case (New Jersey) and Margaret Chase Smith (Maine). These legislators embrace the principle of Social Security financing because President Johnson says "it makes good sense."

We must be queer, because it doesn't make good sense to us; to profoundly disrupt the profession which has provided the richest nation in the world, with the best medical care in the world for much less than its tobacco bill. It doesn't make good sense to us to entrust to government the lever which it has been seeking for so long, in order to socialize the nation; the foot-in-the-door, which once achieved in the name of the aged, will all too soon envelope the entire practice of medicine. And it doesn't make good sense to believe that government can save the taxpayer any money on their medical bills. When did government interest itself in saving money on anything before?

Like the decadent civilization of the past, aware of the danger of social disintegration, but seemingly powerless to stem the tide, we have only our indifference and our own inertia to blame for our present plight. I hope we may never hear in America that futility of futilities "Why didn't our medical societies do something about it before we lost our liberties?"

Morris P. Pitock, M.D.

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172nd ANNUAL MEETING

# of the

CONNECTICUT STATE MEDICAL SOCIETY

Statler-Hilton Hotel
10 Ford Street, Hartford, Connecticut

April 28, 29, 30, 1964

PROGRAM COMMITTEE

Allen M. Margold, *Norwalk, Chairman*
Peter J. Scafarello, *Hartford*
Paul F. McAlenney, Jr., *New Haven*

PRELIMINARY PROGRAM

Tuesday, April 28

Mezzanine Floor

ANNUAL MEETING OF THE HOUSE OF DELEGATES

Michael R. Scully, *Bridgeport, Speaker of the House, presiding*

10:00 Call to Order
Business Session

1:00 Luncheon for Officers, Members of the House and Guests

2:00 Resumption of Business

Wednesday, April 29

9:00 REGISTRATION—MEZZANINE

TERRACE ROOM

9:30 CALL TO ORDER—President of the Society
ADDRESS OF WELCOME—President, Hartford County Medical Association

9:45 SIGNIFICANCE OF FEVER
CHESTER KEEFER, Boston, Massachusetts

10:30 ANTIBIOTICS—PRESENT STATUS AND A LOOK INTO THE FUTURE
LOUIS WEINSTEIN, Boston, Massachusetts

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 MEDICAL ASPECTS OF RENAL HYPERTENSION
JOHN H. MOYER, Philadelphia, Pennsylvania

12:20 PHEOCHROMOCYTOMA
Speaker to be announced

1:00 LUNCHEON—CITY ROOMS
INTERMISSION TO VISIT TECHNICAL EXHIBITS

2:00 TRAGEDY OF THE WASP STING
MARY E. LOVELESS, New York City

2:40 THE PRACTICAL MECHANICS OF MANAGING ALLERGIC PATIENTS IN THE PRIVATE PRACTICE OF PHYSICIANS NOT ALLERGICALLY TRAINED
DOUGLAS JOHNSTONE, Rochester, New York

3:30 **Meetings of Sections of the Society and Guest Organizations**

Section on Dermatology
Section on Gastroenterology (4:30 P.M.)
Section on Internal Medicine (3:00 P.M.)
Section on Neurology }
Section on Neurosurgery } Joint Meeting
Section on Pathology
Section on Physical Medicine
Section on Preventive Medicine & Public Health
Section on Urology
Connecticut Diabetes Association
Hezekiah Beardsley Pediatric Club

7:00 **Annual Dinner of the Society—Terrace Room**

Thursday, April 30

9:00 REGISTRATION—MEZZANINE

TERRACE ROOM

9:45 PROBLEMS IN THE TREATMENT OF CANCER
ALTON OCHSNER, New Orleans, Louisiana

10:30 PRIMARY AND METASTATIC TUMORS OF THE LIVER
GEORGE T. PACK, New York City

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 FACTORS OF RISK IN CLINICAL ATHEROSCLEROTIC DISEASE
WILLIAM B. KANNEL, Framingham, Massachusetts
(Program arranged with Connecticut Chapter—American Academy of General Practice in cooperation with Connecticut Heart Association)

12:20 THE COOPERATION BETWEEN POLICE MEDICAL EXAMINERS AND DOCTORS
MAJOR LESLIE WILLIAMS, Connecticut State Police
(Program arranged with Association of Medical Examiners of Connecticut)

1:00 LUNCHEON—CITY ROOMS
INTERMISSION TO VISIT TECHNICAL EXHIBITS

Program Arranged with the Connecticut Society of American Board Surgeons

2:00 GENERAL SURGICAL PROBLEMS—CASE PRESENTATIONS
MICHAEL E. DEBAKEY, Houston, Texas, Moderator
Panel to be announced.

3:30 Meetings of Sections of the Society and Guest Organizations

Section on Allergy
Section on Anesthesia
Eye, Ear, Nose and Throat Section
Section on Orthopedics (Hunt Memorial Building)
Section on Proctology
Connecticut District Branch—American Psychiatric Association
Section on Radiology
Association of Medical Examiners of Connecticut
Connecticut Rheumatism Association

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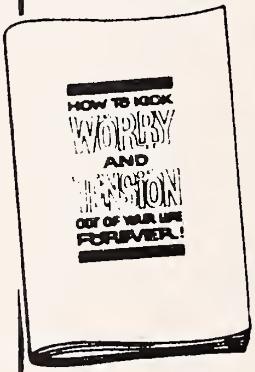

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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1964 Annual Meeting of the House of Delegates will be held at the Statler-Hilton Hotel, Hartford, commencing at 10:00 o'clock in the morning of Tuesday, April 28.

Following luncheon, the House will reconvene for the completion of business.

Morris P. Pitock, President
Michael R. Scully, Speaker of the House
Orvan W. Hess, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENT TO THE BYLAWS

The following proposed amendment to the Bylaws was presented to the House of Delegates on December 11, 1963 and was tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, this amendment will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

INTRODUCED BY THE HARTFORD COUNTY MEDICAL ASSOCIATION

Article VII, Section 1, Paragraph 4 to be amended as follows:

"The Council shall be the Board of Censors of the Society. It shall consider all questions involving the rights and standing of members in relation to other members, to the component associations, or to this Society. In addition, all questions of an ethical nature brought before the House of Delegates or a general meeting, shall be referred to the Council without discussion. It shall hear and decide all questions of discipline affecting the conduct of members of component associations on which an appeal is taken, but only on questions of law and procedure and not on facts and its decision on all such matters will be final.

(a) The Council shall consider only the records of the component medical association in the proceedings involved.

(b) It shall determine that the record available to them is material and sufficient to support the findings which the component medical association reached.

(c) If determining that the above procedure was correct, it shall make its findings known to the appellant.

(d) If, however, finding that the procedure was not material or sufficient, it shall remand the case to the component medical association and ask for a new hearing.

(e) No appeal shall be considered or reviewed until such time as the component medical association has made its decision as to the facts in the case.

The Council shall also serve as a board of review for cases of claimed malpractice referred to it by the Committee on Medical Ethics and Deportment of any component county association."

Delegates To Annual Meeting

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, April 28, 1964, and the Semi-Annual Meeting in December, 1964, is as follows:

COUNTY	MEMBERSHIP DEC. 31,1963	OFFICIAL DELEGATES
Fairfield	907	26
Hartford	1066	31
Litchfield	142	5
Middlesex	122	4
New Haven	952	28
New London	195	6
Tolland	22	1
Windham	67	2

The Secretary's office will appreciate being informed as soon as possible, the names and addresses of all of the delegates who will represent your county at the Annual Meeting of the House of Delegates in Hartford. The Handbook for the meeting will be delivered to each delegate as soon as possible. If any of the delegates from your county association cannot attend the meeting, will you notify this office who their alternates are to be and we shall see that these alternates are supplied with the Handbook and reports.

Election Of Councilors And Associate Councilors

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Fairfield, Litchfield, New Haven and Tolland counties. In accordance with the Bylaws each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Fairfield and New Haven County Medical Associations should elect a Councilor and two Associate Councilors each for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for re-election.

Newly elected Councils and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

* * * *

At the Semi-Annual Meeting of the House of Delegates on December 4, 1962, Article VII, Section 2 of the Bylaws of the Society was amended by the addition of the following sentence after the term Councilor-at-Large:

"In the event that both the Councilor and the Associate Councilor (s) from a county association cannot be present, the President of the county association may appoint a substitute councilor."

COUNCIL MINUTES

Sunday, January 26, 1964

This meeting of the Council was called by the Chairman for the purpose of receiving, discussing and acting upon the notice of the official actions taken by the CMS Corporators at their special meeting on January 23, 1964.

I. Attendance

Present were: Drs. Pitock, Gilman, Cullen, Goldberg, Hess, Weise, Sr., Gardner, Scully, Wilson, O'Connor, Bradley, Martin, Grendon, Grant, Davis, Phillips, Hughes, Shepard, Weber, Jr., Dean, Ciccarelli, Seigle, Egan, Abbot, Caplan, Spitz, Hastings, and Major. Also present: Six physician Members of CMS, Inc.—Drs. M. Caplan, Davis, Denton, Ente, Gallo and Murray, Jr.; Mr. Grant Nickerson of Wiggin and Dana; Mr. James G. Burch; Dr. William R. Richards. Absent: Dr. Gevalt.

II. Special Business

The Chairman opened the meeting by having the General Manager read a letter from W. H. Horton, M.D., Executive Director of CMS, dated January 24, 1964, which informed the Council of the actions taken by the Corporators at their special

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ACCIDENT AND HEALTH PLAN

In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

meeting on January 23, 1964. The pertinent paragraph of the letter read: "Mr. Coolidge (CMS President) wished me to inform you that he read the resolution of the Council, dated January 22, 1964, at the meeting of the Corporation on January 23, 1964, and copies were distributed to the members. Mr. Coolidge also read to the Corporators a formal statement which he had prepared for the meeting, copies of which are enclosed for the members of the Council. Following extended discussion, the Corporators voted to amend the bylaws which was the purpose for which the Special Meeting of the Corporation had been called."

Six physician Members of CMS, Inc. (See "Attendance" above) had accepted the Council's invitation to *all* physician CMS Members to be present at this meeting and the Chairman invited each of them to present his views on the action taken by a majority of the Corporators (10-6) to amend Article I of the CMS Bylaws, and to make suggestions as to how the Council should move in the present situation. Without exception, the six physicians reported that they had "pleaded" with their fellow Corporators to comply with the January 22nd resolution of the Council; i.e., that the Corporation not act to amend the Bylaws as proposed *before* discussing the proposed amendments and related matters with the Council's representatives through a joint meeting of the Liaison Committees of the two organizations, but that their pleas had proven ineffectual in dissuading a majority of the Corporators from voting in favor of adopting the amendments to the Bylaws as proposed. After conducting an informal poll among the six physician CMS Members, the Chairman reported to the Council that five out of six were hopeful that the Council would postpone definitive action in this unfortunate situation until a joint meeting of the two Liaison Committees had been sought once again by the Council to determine whether some reasonable accommodation could not be arrived at between the CSMS and CMS views on the selection of the physician Members of the Corporation.

The amendments to the CMS Bylaws which were under discussion are as follows:

Article I

OLD (2/20/62)

Members

Section 1. *Nominations*: There shall be sixteen Members of the Corporation, at least three of whom must be policy holders. Eight shall be Participating Physicians nominated by the Council of the Connecticut State Medical Society, and eight shall be laymen nominated by a Nominating Committee appointed by the President of the Corporation.

Section 2. *Terms*: Members shall be nominated for two year terms of office, staggered so that the terms of four physician Members and four lay Members will expire at each Annual Meeting.

Section 3. *Resignations*: The Council of the Connecticut State Medical Society may, at any time, obtain the resignation of any physician Director, provided this action be taken for stated cause and that it be supported by at least two-thirds of the membership of the Council.

Section 4. *Vacancies*: Upon the death or resignation of any Member of the Corporation, a vacancy shall be deemed to exist. If the vacancy is that of a physician Member, a nomination to fill the unexpired term shall be requested from the Council of the Connecticut State Medical Society, and, if that of a lay Member, from the Nominating Committee, and the remainder of the Members of the Corporation shall elect his successor in the same manner as provided in Section 1 of this Article. (Note that the word "elect" does *not* appear in Section 1.)

NEW (1/23/64)

Members

Section 1. *Composition*: There shall be sixteen Members of the Corporation, at least three of whom shall be policyholders. Eight shall be Participating Physicians, and eight shall be laymen. (Old Section 1 *Nominations* has been made new Section 3 *Nominations* below.)

Section 2. *Terms*: Members shall be elected for two year terms staggered so that the terms of four physician Members and four lay Members will expire at each Annual Meeting.

Section 3. *Resignations* has been deleted. New Section 3 reads:

Section 3. *Nominations*: The President shall appoint a Nominating Committee composed of two physician Members and two lay Members who shall make all nominations for membership in the Corporation.

Old Section 4. *Vacancies* has been deleted and replaced by new Section 4 *Elections* which reads:

Section 4. *Elections*: Each person whose name is proposed by two or more Members of the Nominating Committee shall be deemed nominated, and if there be two or more nominees for any membership, all of the Members of the Corporation, including those whose terms expire at the conclusion of the meeting shall vote upon the same by written ballot.

It was emphasized that the "agreement" between CSMS and CMS as to the naming of the physician Members of the Corporation which was written into the old Bylaws has been entirely eliminated by the amendments adopted by the CMS Corporators on January 23, 1964.

Mr. Nickerson presented the Council with three possible courses of action which might be taken with respect to the present situation:

(1) The Council may continue to pursue the possibility of achieving reasonable accommodation of the CSMS and CMS attitudes toward the naming of members and directors of CMS through the medium of further liaison meetings.

(2) The Council may find that, in effect, a majority of the Members of CMS have made it clear that they will allow the Council nothing more than the right to "suggest" the physician Members of the Corporation, and that such a limited power to nominate is considered to be inconsistent with continuing sponsorship of CMS, Inc. by the Connecticut State Medical Society.

(3) The Council may wish to attempt to establish (through further court action) the right of the four physicians named as CMS Members by the Council on January 22nd to be seated as members and directors of CMS at the Annual Meeting of the Corporation on February 18, 1964, the amendments to the CMS Bylaws adopted on January 23rd notwithstanding.

Of these three possible courses of action, Mr. Nickerson favored pursuing the first one initially unless the Council is convinced already that the second course can be justified completely without further liaison discussions. The third course he feels would be expensive and, even if successful, would only delay any possible final settlement of the present controversy.

After weighing these and other points of view, and subsequent to prolonged discussion of the many problems and possible pitfalls associated with this complex problem, the following positive actions were VOTED:

(1) IT IS MOVED: That, since it is possible that CMS may still be willing to engage in further discussions concerning amendments to the CMS Bylaws, the Council direct its Chairman to communicate with the President of CMS, Inc. for the purpose of arranging a joint meeting of the Liaison Committees of the two Corporations, and that the communication include suggestions as to the conducting of such a liaison meeting which will reflect the views of the Council expressed at this meeting.

(2) IT IS MOVED: That the Council direct its Liaison Committee to report unfavorably to the Council on any alternative plan (for the naming of Members of CMS) that is in conflict with the Council's minimum requirement that the physician Members of CMS, Inc. be chosen from among those designated by the Council of the Connecticut State Medical Society.

(3) IT IS MOVED: That the Chairman be directed to appoint a committee to immediately draw up the mechanics of informing the CSMS membership of the situation as it now stands with CMS, Inc., so that the council may move from a position of strength (with the membership informed) and not of ignorance (of the membership as to the present situation).

Dr. Martin appointed the Committee as follows: Drs. Pitock, Richards and Martin.

In response to a request for direction made by several members of the CSMS Liaison Committee with CMS, the following suggestions were offered:

(1) That, unless objected to by CMS, Mr. Nickerson accompany the Council's representatives to the joint meeting of the Liaison Committees when it is held.

(2 That the CSMS liaison group should advance points of view on behalf of the Council along the following lines: (a) That the Council would look with disfavor on any plan which was in conflict with the "minimum requirement" stated in the motion (above) which was adopted by the Council at this meeting; (b) that the Council insists that its "right of recall" for cause be restored to the CMS Bylaws; and (c) that the Council is in favor of discussing the desirability of having all Members of CMS, Inc. "elected" in a uniform manner.

It was noted that in Dr. Horton's letter of January 24, 1964, Mr. Coolidge had wished to notify the Council that the Executive Committee of the Corporation would "as soon as possible" be asked to meet to act upon a resolution dealing with a future joint liaison meeting, but it was agreed that this notice was information only and did not constitute an invitation from the Corporation to the Council to join with the CMS Executive Committee in such a liaison meeting.

N.B.: *The foregoing is a summary of the proceeding and actions of the Council on January 26, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

In Memoriam

Dillon, John H. – Waterbury, Yale Medical School, 1904. Dr. Dillon was a practicing physician in Waterbury for 55 years. Dr. Dillon served on the staff of St. Mary's Hospital from the time the hospital was founded until he retired as a practicing physician. Dr. Dillon's service of more than a half-century in the medical field was given recognition in 1960 by the Connecticut State Medical Society, of which he was a member. He was former president of the Waterbury Medical Association and a member of the American Medical Association. Dr. Dillon died January 27, at the age of 83.

DuBois, Robert L. – Waterbury; University of Maryland School of Medicine, 1936. Dr. DuBois was a prominent eye, ear, nose and throat specialist in Waterbury for many years. Dr. DuBois was a Lieutenant Commander in the Navy Medical Corps from 1943 to 1946, which included two years in the Pacific Theater and the invasions of Leyte and Okinawa. Dr. DuBois was the attending eye service physician at the Waterbury Hospital for many years and up until the time of his illness. He was also the attending eye, ear, nose and throat physician at St. Mary's Hospital and served as president of St. Mary's staff during the hospital's jubilee year of 1949. Dr. DuBois was a member of the Waterbury Medical Association, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a fellow of the American College of Surgeons. Dr. DuBois died January 26, at the age of 54 .

Felty, Augustus R.—Old Saybrook; Johns Hopkins University, 1920. Dr. Felty had been a member of the Hartford Hospital staff and a consultant at the Veteran's Administration Hospital, Rocky Hill; the Institute of Living, Hartford; the Charlotte Hungerford Hospital, Torrington; the Middlesex Memorial Hospital, Middletown; and the New Britain General Hospital, New Britain. He was a charter diplomate of the Board of Internal Medicine and a member of the Connecticut State Medical Society, the American Medical Association, the American Rheumatism Association, and a fellow of the American College of Physicians. Dr. Felty died February 4, at the age of 68.

Fischer, Alexander – Hamden; University of Paris, 1936. Dr. Fischer was a practicing physician in Hamden for 19 years. Dr. Fischer was on the staffs of the Grace-New Haven Community Hospital and the Hospital of St. Raphael and was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of General Practice. Dr. Fischer died January 13, at the age of 56.

Kendall, Ralph E. – Hartford; Johns Hopkins University Medical School, 1921. Dr. Kendall was a long time pathologist and bacteriologist at the Hartford Hospital, the Manchester Memorial Hospital and the Municipal Hospital, near McCook Memorial Hospital. He was an Army veteran of World War I and technical director of the Hartford Red Cross Blood Donor Service during World War II. He organized the Hartford Hospital cytology center, the first one in the state, in 1946, under a Cancer Society grant. Dr. Kendall received the Cancer Society's Bronze Medal for his cancer research work. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American College of Physicians, the American Society of Clinical Pathologists, and the New England Cancer Sociey. Dr. Kendall died January 28, at the age of 68.

O'Donnell, Thomas J. – Greenwich; Syracuse University Medical School, 1908. Dr. O'Donnell was a practicing physician in Greenwich for nearly 54 years. He was associated with the staff at Greenwich Hospital. Dr. O'Donnell was a member of the Greenwich Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. O'Donnell died February 4, at the age of 79.

Patterson, Frederick A. – Norwalk; Harvard Medical School, 1927. Dr. Patterson was a practicing physician in Norwalk for 35 years. He served in England and France as a Major in the Army Medical Corps during World War II. Dr. Patterson was a member of the attending surgical staff at the Norwalk Hospital. He was a member of the Norwalk Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Patterson died February 1, at the age of 63.

Serafin, Peter J.—North Haven; New York University College of Medicine, 1921. Dr. Serafin was a well known physician and surgeon in the New

Haven area for 41 years. During World War II he was examining physician of Draft Board IIB and for his services was awarded the Selective Service Medal by President Harry Truman. He was appointed by Mayor Lee to the Board of Fire Surgeons, serving for several years until ill health forced him to resign. Dr. Serafin was assistant attending in surgery at St. Raphael's Hospital and was also on the staff of the Grace-New Haven Community Hospital. Dr. Serafin was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American College of Surgery, and the New York Academy of Sciences. He was a diplomate of the International College of Surgery, United States Chapter, and a fellow of the American College of Gastroenterology. Dr. Serafin died February 4, at the age of 73.

SPARTEINE SULPHATE

Sparteine sulphate should no longer be considered a completely safe or innocuous drug. This is amply demonstrated by a recent survey of hospitals of the State of Connecticut. Sparteine sulphate may produce varying degrees of uterine contractions—in the pregnant uterus— similar to all oxytocic drugs— and all such drugs have caused tetanic contractions. Rupture of the uterus, fetal distress and resultant fetal death have occurred following administration of sparteine sulphate.

In the light of this study, it is the judgement of the Committee on Maternal Morbidity and Mortality of the Connecticut State Medical Society that sparteine sulphate should not be given to an obstetrical patient except under strict obstetrical supervision. It is our opinion that rules should be set up in the individual obstetrical services that are identical with those governing the use of intravenous syntocinon or pitocin.

Dosage Schedule

The dosage schedule is emphasized. If satisfactory uterine contractions are not obtained afte1 the initial dose of 1 cc., another 1 cc. dose may be administered after 1 hour. Repeated doses, when required, may be administered at 1½ to 2 hour intervals to maintain satisfactory uterine stimulation, until a total of 4 doses (400 mgm.) have been given. An initial dose of ½ cc. followed by ½ cc. in 30 minutes to evaluate the patient's initial response has great merit.

Warning

When combinations of sparteine sulphate and pitocin or syntocinon are used, the patient must be even more carefully observed for sensitivity due to the known synergistic or augmentation action of sparteine sulphate, plus another oxytocin, which may result in tetanic uterine contraction. It has been shown in isolate muscle strips of the term pregnant uterus that sparteine sulphate followed by pitocin or syntocinon produces three times as many tetanic contractions as either drug given alone. The sequence of pitocin or syntocinon causes only somewhat less frequent tetanic contractions. Therefore, such combinations probably should not be used in any one 8-hour period in any one patient.

Contraindications

The contraindications to the use of sparteine sulphate are:

1. Heart disease, acquired or congenital, active or inactive
2. Grand multiparity
3. Active labor
4. Labor where there is any suspicion of hypertonic or tumultuous uterine contractions
5. Cephalopelvic disproportion
6. Previous abdominal deliveries
7. Uterine scars
8. Placenta previa
9. Abruptio placenta
10. Trial of labor
11. Elective induction of labor when the obstetrical conditions are not favorable

Hugh K. Miller, M.D., Chairman
Committee on Maternal Morbidity and Mortality of the Connecticut State Medical Society

Doctor's Office

Clemens E. Prokesch, M.D. announces the removal of his office for the practice of internal medicine from 58 Huntington Street, New London to 435 Montauk Avenue, New London.

Charles D. McCullough, M.D. announces his association with Drs. Jules S. Terry and Harry A. Inder for the practice of obstetrics and gynecology at 2685 Main Street, Bridgeport.

WOMAN'S AUXILIARY

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Attention Auxiliary Members

The Annual Meeting of the Woman's Auxiliary to the Connecticut State Medical Society will be held in Hartford on Wednesday, April 29, 1964. Time and place to be announced at a later date.

1964 National Convention

San Francisco, California will be the setting for the 1964 convention of the Woman's Auxiliary to the American Medical Association. Convention dates are June 21-25 and headquarters will be at the St. Francis Hotel on Union Square. Registration for this convention will open at 11:00 a.m. on Sunday, June 21st. The annual tea and fashion show honoring Mrs. C. Rodney Stoltz and Mrs. William H. Evans will be held from 4 to 6 o'clock on Sunday. All members are urged to attend. Tickets will be $3.50 including tax and gratuity. The program will feature chinese robes and show how these exotic ceremonial costumes can be adapted to modern western wear. The creations will be modeled both by beautiful Chinese and Occidental mannequins. Advanced reservations for this tea can be made through Mrs. Alfred A. deLorimier, Ticket Chairman for Convention, 103 Font Boulevard, San Francisco 27, California. The headquarters hotel, St. Francis, and the Sir Francis Drake Hotel have set aside a limited number of rooms for the Auxiliary, available on a first come first served basis. Reservations should be made on the official AMA housing form.

Darien Book Aid Plan

County Chairmen and members of the Auxiliary are continuing to collect magazines and text books for hospitals, clincs and medical schools overseas. This is done through the Darien Book Aid Plan which has processed and shipped approximately one-half ton of this material during the past three months.

At the present time a box is being prepared for Dr. Eugene Chan in Hong Kong. This will contain up-to-date material on ophthalmology, and although Hong Kong is not presently on the list of recipients, a special effort is being made to get the books to Dr. Chan becuse of the extreme need for these books.

Because of the growth of this plan it is impossible for members of the Darien Book Aid Plan to collect the books and magazines from individuals or counties. Responsibility for getting the material to Darien must be taken by the county International Health Activities Chairmen.

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Think of the surviving family members. The survey found that of the 144 deceased doctors included in the study:

- *34% had left no will*
- *13% were in debt at the time of death*
- *31% left net estates of less than $10,000*
- *62% were survived by their wives and families.*

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Letter To The Editor

Parnate, Headache and Cheese

To the Editor:

It has been known for some time that tranylcypromine (Parnate) and other monoamineoxidase inhibitors occasionally cause severe headache. More recently, reports have appeared in the English literature of patients, who, while being treated with Parnate, sometimes complain of extremely severe headache after eating cheese. Inasmuch as I have been unable to find any reports in the American literature on this concurrence, it is felt that a short clinical report of one case is in order, to alert the readers of this Journal to this complication.

Mr. G. S., a thirty-nine year old business man, has suffered during the past three months from a mild reactive depression which is characterized by anxiety, restlessness, loss of self confidence, lack of drive, insomnia, diminished appetite, no weight loss, poor work output and crying spells. The patient feels rather hopeless about his present condition, both moodwise and as regards his professional status, but he denies suicidal preoccupation.

He has been treated with tanylcypromine starting on 8/23/63, 30 mgms daily; this was increased within four weeks to 50 mgms daily, and on 10/9/63 the dosage was increased to 60 mgms daily. On 10/16/63 the dosage was reduced to 30 mgms daily after he had reported the occurrence of headache. He received also trifluoperazine (Stelazine) 2 mgms daily and Doriden 1.0 gram, h.s. On this regimen improvement has been fairly satisfactory in that the patient has continued to go to work and the depression has lifted gradually. The patient has had severe headaches on two occasions during the time when he was taking from 50 mgms to 60 mgms of Parnate daily. He described the headaches as agonizing, excruciating, localized in the occipital region, with pounding and throbbing of the entire head and particularly of the temples. He had a feeling as if he were going to have a cerebral hemorrhage. He did not faint, there was no chest pain. On both occasions he was pale, which pallor was described to him by his wife and by his secretary; he had cold sweats and he was slightly nauseated. On the first occasion the headache lasted for two hours and in the second instance it continued for better than one hour. The cephalalgia was less severe when standing up and while walking about, but it increased when he sat down and on lying down the headache was unbearable. Unfortunately, there was no opportunity to take the patient's blood pressure during the time when he had these headaches. Several blood pressure readings at times when he was entirely free from headache revealed the commonly occurring mild hypotension in patients who are taking monoamineoxidase inhibitors. There was no evidence of orthostatic hypotension; the blood pressure was in the lying down position, 100/64; sitting up, 108/78; and standing up, 90/60.

On both occasions when the patient experienced the typical headache syndrome, he had eaten a Cheddar cheese grilled sandwich for lunch and the headache started approximately one hour after he had eaten these lunches. He decided, quite on his own initiative, to eliminate cheese from his diet and he has not suffered from headache since, although treatment with Parnate has been continued. He felt so foolish to attribute headache to eating cheese that he did not mention this sequence of events to me until I told him not to eat cheese while he was on Parnate.

Three practical considerations come to mind in connection with this case and when one peruses the literature. First, it points up how important it is to listen carefully to our patients. A psychological reaction of disbelief, so vividly experienced by my patient, was described by one of Read's[1] patients, however, not within herself but in a group of doctors. She suffered severe headaches while on Parnate and after eating cheese. The occurrence of this complication of the treatment was apparently common knowledge among the group of patients with whom she was hospitalized and who were treated with the same drug. She wrote as follows: "Other patients having Parstelin experienced this as well after cheese, but the doctors laughed at the idea."

Secondly, it may be well for physicians who are treating patients who complain of headache to keep in mind that some of the modern psychotropic drugs may cause exceedingly severe headache and that the ingestion of cheese may very well be an important contributory factor in bringing about the typical headache syndrome. And thirdly, on the basis of the evidence so far available, it seems wise and prudent to give our patients the advice to eliminate cheese from their diet while they are being treated with monoamineoxidase inhibitors.

Sincerely yours,

Adrian C. Moulyn, M.D.

Stamford, Conn.

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[1] Read, A. E. A. and Arora, B., Lancet 2: 587 (Sept. 14) 1963.

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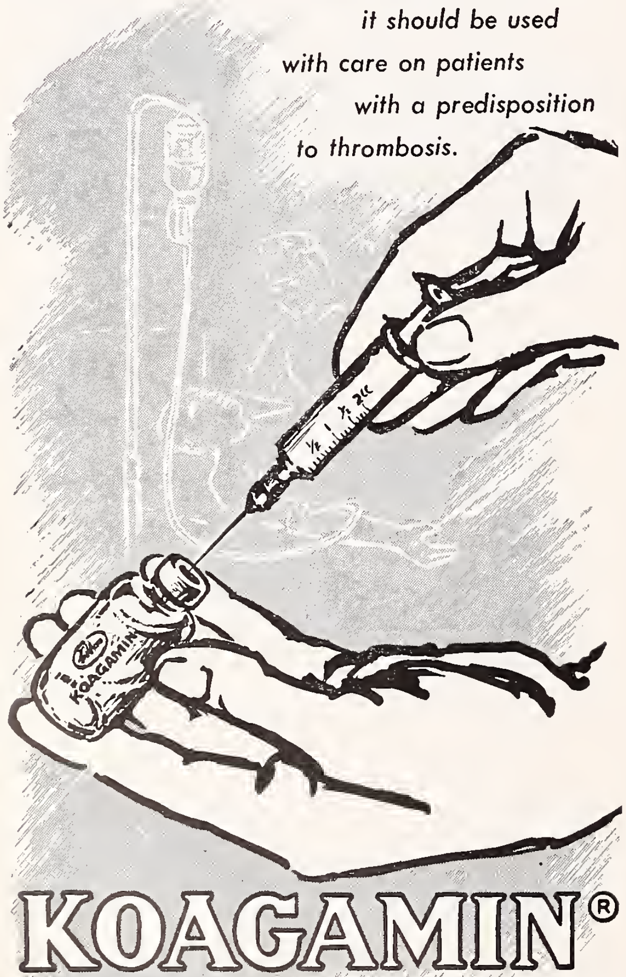

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Around The State

New Haven County

The 180th Annual Meeting of the New Haven County Medical Association will be held at the Waverly Inn, Meriden, on Thursday, March 19, 1964 at 2:30 P.M., the time scheduled for the Business Meeting.

The agenda for the business portion of the meeting includes the election of Officers, Committee and Alternate Delegates for the year 1964-1965.

A social hour and dinner with the members of the Woman's Auxiliary will follow the business meeting. The retiring President will be presented with the usual inscribed placque following the dinner.

Members elected at the Semi-Annual Meeting in October will be guests of the Association. They will be introduced and requested to sign the Indoctrination Roster at this time. Dinner is scheduled for about 7:00 P.M.

The after dinner program, arranged by Program Chairman, Dr. Stewart Petrie, will include lecture and slides by Dr. Alan S. Dana, United States Public Health Service, Communicable Disease Center, Atlanta, Georgia who will speak on "Dog Sled Epidemiology".

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PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

Ali Akbari, age 36 — M.D. Lausanne, Switzerland 1957. Four years residency training in approved medicine in Internal Medicine. Desires employment of any kind while waiting for his citizenship.

David Marzouk, age 34 — M.D. Cairo University 1957. Specialty: Obstetrics and Gynecology.

Howard M. Levine, age 30 — M.D. University of Louisville School of Medicine 1957. Specialty: Obstetrics and Gynecology.

Pathologist, age 30 — M.D. University of Buffalo School of Medicine 1959. Connecticut license.

PLACEMENT OPPORTUNITIES

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BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Current Pediatric Therapy by Sydney S. Gellis, M.D., and Benjamin M. Kagan, M.D., W. B. Saunders Co., Philadelphia, Pa., 1964, 747 pp. $16.00.

Current Diagnosis Treatment by Henry Brainerd, M.D., Sheldon Margen, M.D. and Milton J. Chatton, M.D., Lange Medical Publications, Los Altos, California, 870 pp. $9.50.

Medical Pharmacology Principles and Concepts by Andres Goth, M.D., The University of Texas Southwestern Medical School, Dallas, Texas, 1964. 546 pp. $11.75.

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Special Notices

HARTFORD HOSPITAL

SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS

March 6 to April 25, 1964

March 6-7—*Martin Netsky, M.D.*, Prof. of Neuro-Anatomy. Univ. of Virginia.

Mar. 6—"Neurosecretions," Newington V. A. Hospital

Mar. 7—11:00 a.m., H.H. Amphitheater

Subject: "The Art of Taking a Test" ("How To Get A Better Score Without Knowing Any More")

March 14—*George Ludwig, M.D.*, Assoc. Prof. of Medicine, Univ. of Penn.

Subject: "Some Problems of Calcium and Phosphate Metabolism"

March 21—*S. N. Bhaskar, D.D.S., M.S., Ph.D.*, Chief, Dept. of Oral Pathology, U.S. Army Institute of Dental Research, Walter Reed Army Med. Center.

Subject: "The Mouth and Systemic Disease"

March 28—*Symposium on Hypertension*
10:00 a.m. to 12:00 p.m., H.H. Amphitheater
Albert A. Brust, M.D., Assoc. Prof. Clin. Med., Cincinnati
Arthur C. Corcoran, M.D., Chief, Dept. Clin. Investigation, St. Vincent Charity Hosp., Cleveland
Robert L. McMillan, M.D., Director Heart Station; Prof. Clin. Medicine, Bowman Gray

April 4—*Nicholas P. Christy, M.D.*, Assoc. Prof. of Medicine, Columbia P & S

Subject: "Problems of Steroid Withdrawal"

April 10-11—*Joseph Beninson, M.D.*, Dermatologist, Henry Ford Hospital, Detroit.

April 10—3:30 p.m., "Varicose Veins," Newington V.A. Hospital

April 11—H. H. Amphitheater

Subjects: 9:00 a.m.—"Conservative Management of Varicose Veins"
10:00 a.m.—"Management of Varicose Veins in Obstetrics and Gynecology"
11:00 a.m.—"The History and Management of Varicose Veins"

April 18—*Lyon P. Strean, Ph.D., D.D.S.*, Asst. Dir. of Med. Communications, Merck, Sharp & Dohme, West Point, Penn.

Subjects: 10:00 a.m.—"Basic Information Relating to Acquired and Hereditary Congenital Defects"
11:00 a.m.—"Clinical Geno-Dermatoses"

April 24-25—*D. Murray Young, M.D., Ph.D.*, Director of Laboratories, Toronto General Hospital.

Subject: "The Importance of Quality Control To The Patient, His Physician and the Community"

COMPREHENSIVE CARE OF THE AGED

April 15, 1964

St. Joseph's Manor
6448 Main Street
Trumbull, Connecticut
12 noon — Luncheon
Speaker: Reverend John Lynch
2:00 to 5:00 P.M. — Panel Discussion

Howard Rusk, M.D., New York University—Rehabilitation.

Francis Braceland, M.D.—Institute Of Living, Emotional Problems.

Jere Lord, Jr., M.D., New York University—Cardiovascular.

CONNECTICUT DIABETES ASSOCIATION, INC.

Statler Hilton Hotel, Hartford, Conn.
April 29, 1964
3:30 P.M. — Room 440

Speaker: Dr. Harold Rifkin, Clinical Professor of Medicine, Albert Einstein College of Medicine.

Subject: "Current Problems in Diabetic Microangiopathy."

1964 MEETINGS

March 19 — 180th Annual Meeting of the New Haven County Medical Association will be held at Waverly Inn, Cheshire, Conn. Business Meeting scheduled for 2:30 P.M.

April 28-30—Annual Meeting Connecticut State Medical Society, to be held at Statler-Hilton Hotel, Hartford.

May 20—Annual Meeting Connecticut Heart Association to be held at Hillandale Country Club, Trumbull.

May 25-27—Annual Meeting American Thoracic Society Medical Section of the National Tuberculosis Association to be held in New York City.

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

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BOOK REVIEWS

CLINICAL EXAMINATIONS IN NEUROLOGY by Members of the Sections of Neurology and Section of Physiology, Mayo Clinic and Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minnesota, Second Edition, W. B. Saunders Co., Philadelphia, Pa., 1963, 396 pp., $8.50.

Reviewed by: LOUIS H. NAHUM

This is a collaborative book of fifteen members of the section of neurology and the section of physiology of the Mayo Clinic. So perfectly is anatomy, physiology and neurology integrated, that one cannot tell who wrote what. But it is at once apparent from the logic and completeness and homogeneity of the presentation that the advantages of a group of doctors working together for the care of the sick are many.

The senior author speaking for the rest states that the book is dedicated to Henry W. Woltman and Frederick P. Moersch from whom they learned the techniques and judgments necessary to their craft by performing, instead of merely assimilating by rote. Obviously, they learned more than just performing. They learned to work together in harmony and co-operation "free of jealousy, greed and false pride." It is no wonder then that this book has everything that can come from the co-operation of good minds.

There are nineteen chapters, the first on neurologic history, a second on the use of various forms for recording a history, and the results of clinical examinations. Then successively on every aspect of the examination of sensory and motor function; mental function, language and motor speech; a chapter on clinical examination in selected problems of pain; one on neuroradiologic procedures, one on electroencephalography, one on electric stimulation of peripheral nerves and muscle. There is an excellent chapter on biochemical and pharmacologic aids in neurologic diagnosis and a final chapter on the examination of cerebrospinal fluid by lumbar and cisternal puncture. The chapter on neuroradiologic procedures is new and the neurologic examination of infants has been much expanded over that in the first edition.

This book should be in the hands of internes, residents, physicians who wish to understand and perform a neurologic examination. It is a first class product in a co-operative effort from a great clinic.

DISEASES OF THE KIDNEY, Edited by Maurice B. Strauss, M.D. and Louis G. Welt, M.D., Little, Brown and Company, Boston, 1963, 43 contributors, 1033 pp., illustrated, $32.50.

Reviewed by: ROY N. BARNETT

This comprehensive, well-written and authoritative volume can be considered as the definitive work on the kidney. In most of the many fields covered there is an up-to-date and critical discussion adequate for the ordinary needs of any physician or medical student. For those who wish to pursue individual topics further there is a thorough bibliography at the end of each chapter.

In the first chapter Johannes Rhodin gives an intimate insight into the finer structure of the kidneys and illustrates this with magnificent electromicrographs. There are portrayed many structural minutiae whose presence was presumed but not demonstrated before the high magnification era.

Chapter II, in which Robert Berliner covers renal physiology in only 48 pages, is an amazingly lucid exposition of a complex subject. He even makes the principles of the counter current exchanger and multiplier comprehensible (at least while you are reading the section!)

The third of the basic chapters is concerned with the clinical examination of renal function. Relman and Levinsky give a common-sense treatment of the subject with sufficient detail to permit utilization of recommended techniques by interested physicians.

There are a number of chapters dealing with specific types and aspects of glomerulonephritis, nephrosis, pyelonephritis, nephropathies of metabolic origin, nephrolithiasis, etc.; and excellent discussions of such relatively unfamiliar entities as medullary cystic disease and the renal lesions of scleroderma. Among the very good chapters are two written by members of the Yale faculty well-known to most Connecticut physicians, that on Nephropathy of Hypercalcemia by Franklin Epstein, and on Pyelonephritis and Urinary Tract Infection by Lawrence Freedman. Among the other contributors who received at least part of their training at Yale in the John P. Peters era are Jack Orloff, Arnold Relman, Donald Seldin and, of course, Louis Welt.

Particularly practical for the practitioner are the two chapters by John Merrill; one on Dialytic Methods of Treatment and one on Acute Renal Failure.

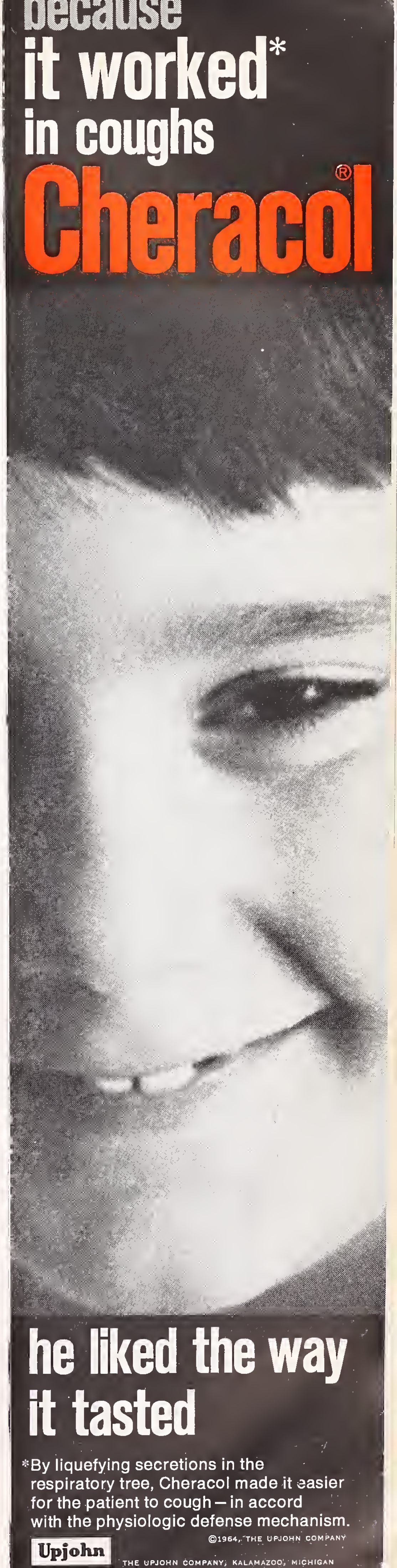
It would be surprising if every chapter was of the same uniform excellence. There are two which struck me as below average. One is entitled the Kidney in Gout, by John Talbott and Kornel Terplan. It is lavishly illustrated with expensive color photomicrographs of inferior quality; these show much less detail than good black and white pictures and could well be replaced in future editions. The other is on Tumors of the Kidney by J. Hartwell Harrison. It says little more than similar sections in various Pathology Textbooks for second-year medical students, avoiding any critical analysis or controversial areas. If a chapter on renal tumors is truly part of the subject matter one could expect a far longer, more comprehensive and critical discussion than is presented.

This book should be in every hospital and medical school as a reference work. It is highly recommended for any physician who wishes to understand our current areas of knowledge, ignorance and controversy in the field of renal disease.

HYPERTENSION, VASOACTIVE MECHANISMS, Vol. XI, Proceedings of the Council for High Blood Pressure Research of the American Heart Association. Simon Rodbard, M.D., Editor, American Heart Association, New York, N. Y., 1963, 93 pp. $2.50.

Reviewed by: HERBERT LEVINE

This monograph consists of six papers concerned with mechanisms affecting the vasomotor control of blood pressure presented at the meeting of the Council for High Blood Pressure Research in Cleveland in October, 1962, together



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with the discussion that followed their presentation. As such they afford an interesting insight into several current approaches to the etiology of hypertensive diseases. Phyllis Hartoft reviews the evidence that the renal juxtaglomerular cells are involved in a secretory sense with levels of humoral pressor agents, and that they actually secrete renin. Hyperactivity of these cells is seen in hypoadrenal states, decreased blood pressure, renal ischemia, edematous states, and hyponatremia. High potassium intake, however, did not affect their activity in experimental studies. The relation of the renin-angiotensin system to aldosterone secretion is mentioned only briefly.

Braunwald and co-workers describe an ingenious set of experiments designed to illustrate effects of various agents on venomotor tone. In anesthetized, open-chest dogs on cardio-pulmonary bypass, a number of modifications of venous tone were effected. Venoconstriction was seen in response to infusion of epinephrine and nor-epinephrine; lowering of pressure on carotid, left atrial, and left ventricular baroreceptors; and hypoxia. Venodilitation was produced by trimethaphan and by stimulation of the carotid and left heart receptors. Reflex venoconstriction appeared in response to carotid occlusion, but this response could be blocked by guanethidine and reserpine. These mechanisms would appear to be of importance in the regulation of cardiac output and hence of arterial pressure.

McCubbin and Page present evidence that angiotensin in very small amounts enhances the response of the sympathetic nervous system to agents and procedures the cause release of endogenous nor—epinephrine, and this may account for the large neurogenic component of renal hypertension. Taquini discusses experiments which indicate the importance of the central nervous system in maintaining the increased peripheral resistance of renal hypertension.

Rosas discusses the properties of a vasoactive peptide, anephrotensin, obtained by acid incubation of serum. It is not activated from its precursor by renin, as is angiotensin, but the concentrations of the two substances change in parallel fashion in experimental nephrectomy and treatment with desoxycorticorsterone acetate. He suggests that the renal handling of these substances and their substrates may be involved in the production of their hypertensive effects.

Peterson, in the last paper, attempts to place the many factors related to regulation of the mechanical properties of the arterial wall in a block diagram arrangement, and to suggest the "feed-back" nature of their interactions. The mathematics and physics involved are rather complex, but the diagram itself affords a useful general picture of the manifold influences on arterial tone.

The entire monograph will provide the physician interested in hypertension with insight into a number of recent and interesting experimental approaches to the mechanisms regulating blood pressure and their interactions.

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Medical Aspects Of Nuclear Warfare: II—Marshall Brucer, M.D., *Guest Editor*

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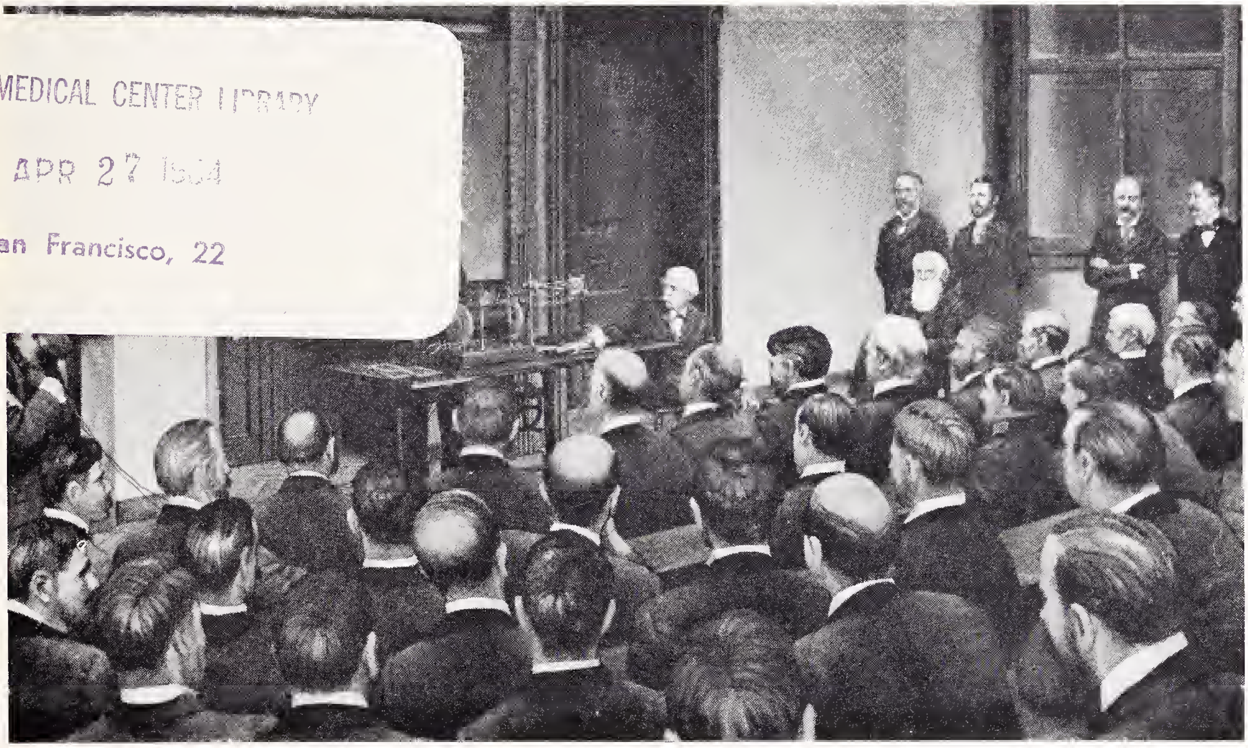

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RÖNTGEN: INVISIBLE RAYS SAVE LIVES (see page 237)

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*Roseman, E.: *Neurology* **11**:912, 1961. 33664

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Connecticut Medicine

editorials

Should Scientists Stand Aside?

> *Our reason may be a pitiful candle light in the dark and boundless sea of being, but we have nothing better and woe to those who wilfully try to put it out.*—Morris Cohen, Reason and Nature.

The forces unleashed by science are incomparably powerful. Thus, scientists who make science, have become the most important occupational group in the world today. What they do is of immediate concern to the whole of human society. Intellectually they have transformed the climate of our time. Socially, science will decide whether and how we live or die. Is it right then that scientists should stand aside and say "we produce the tools," and stop there. "Let the rest of the world, politicians, statesmen, say how these tools are to be used." But the tools may be used for purposes which most of us regard as bad. Is this or is it not a concern of the scientist? There is only one answer to this question according to Sir Charles P. Snow,[1] science and scientists cannot be morally neutral.

The desire to find the truth is the quintessence of morality. Truth is what makes science work. It is what scientists are trying to find out. Without truth there could be no science. If you are going to find "what is there" you can't deceive yourself or anyone else. No fraud or honest mistake stays undetected for long, because criticism is inherent in the process itself. Science is thus a self-correcting system and compels the scientist to have a respect for truth at every stage in the investigation. An overwhelming number of scientists keep to the truth, and this is a demonstration for anyone to see of moral behavior on a very large scale. We take this for granted. To us it is absolutely clear. Yet, it is important because it differentiates science from all other intellectual activities. Snow calls it "a built-in moral component right in the core of the scientific activity itself." Because the desire to find the truth is itself a moral impulse, the way in which a scientist tries to find the truth imposes on him a constant moral discipline. If the scientific activity contained only this one moral component, that alone would be enough to let us say that it was morally un-neutral.

This kind of activity stamped the scientific world of the twenties as a full fledged international community. It was filled with an air of benevolence and magnanimity says Snow which transcended the people who lived in it. The scientists lived on a plane above the nation-state and lived there with joy. Peter Kapitza, a loyal Soviet citizen worked for many years in Rutherford's laboratory before returning to his native land and while in England he became a Fellow of the Royal Society and founder of the best physics club Cambridge has ever known, Pavlov travelled extensively and in 1929 came to this country where I and many others had the edification of being with this giant among physiologists.

The Kapitza phenomenon couldn't take place now since we are suffering from the tempest of the second World War which brought forth a technological tempest too. The discovery of atomic fission broke up the world of international physics. Once fission was discovered and some technical break-throughs in electronics, physicists have been faced with a bitter task. Overnight they became the most important military resource, soldiers, though not in uniform, and so they have remained.

THE COVER

RÖNTGEN: INVISIBLE RAYS SAVE LIVES

AT HIS first public demonstration of newly discovered X-rays, the evening of January 23, 1896, Wilhelm Conrad Röntgen (1845-1923) astounded scientists who filled the room. Professor of Physics and Rector of the University of Würzburg, Germany, Röntgen completed his demonstration by taking an X-ray photograph of the hand of the famed Professor of Anatomy, Albert von Kölliker. This led to discussion of possible medical applications. The news traveled fast, and within a year, X-ray equipment was being employed by medical men around the world as a diagnostic tool. Later research revealed many therapeutic, commercial, and industrial applications, as well as the hidden dangers, of X-rays.

It was right for them to do so during the Hitler war, since Nazism was as near absolute evil as a human society can manage to become, and the nightmare of Hitlers scientists producing "the bomb" was so real that there was nothing else for physicists to do. But when the scientist became a soldier he gave up something of the full scientific life. Soldiers have to obey, that is their morality. This erodes part of the scientists purpose to question and when necessary to rebel. As Snow points out, the long and gloomy history of man reveals far more hideous crimes committed in the name of obedience than have ever been committed in the name of rebellion. The German Officers Corps were brought up in a rigid code of obedience and so they were party to and assisted in the most wicked and large scale murders of innocent human beings in the whole history of mankind.

Scientists must not go that way. They have a duty to question, but it is not much of a support when you are living in the middle of an organized society with a "moral trap," hiding behind an institution where you lose the power to say no. One has to be bold to say no, because it often means to stand alone, to be away from your other colleagues, and not too many scientists will do this. Nevertheless, in the search for truth, scientists obtain knowledge. They know certain things in a more certain way than those who don't comprehend what science is. This knowledge is bound to shape our action to give us "guts."

All physical scientists know that it is easy to make plutonium, that in a few years a dozen or more states will make "the bomb." This is an engineering truth. We know that if enough different states have this weapon, some are going to go off, through accident, folly or madness. We know this in a more direct sense than any politician. Because we know this better than anyone, it throws a personal responsibility upon scientists. They have a moral imperative to say what they know. It may make them unpopular, but in the face of the risks, this must not be allowed to count.

Clearly we have not much time. Either we accept a restriction on nuclear armament in which there are some risks, or else be faced with a nuclear arms race that will accelerate as other countries join in. Soon China and other countries will have the bomb. Then some will go off, this is a certainty. On one side there is a finite risk on the other side certainty of disaster for the human race. Between a risk and a certainty a sane man cannot hesitate From the moral nature of scientific activity comes the plain duty of scientists to explain this either-or.

The same duty in a much more pleasant form arises with respect to the benevolent powers of science. We know with certainty that we possess every scientific fact to transform the physical life of half the world so that they will live as long as we do, suffer no more than we do and eat enough. It is within our power to start on this problem, we are morally impelled to. True, as these problems are solved others will arise such as "population explosion," but a challenge is not an excuse for slinking off and doing nothing. For the above reasons, since science is involved in these problems, the community of scientists has a final responsibility upon it. How will they bear this responsibility, stand aside, or tell what they know?

L.H.N.

Reference

1. Snow, C. P.: The moral unneutrality of science. Science 133: 225, (Jan.) 27, 1961.

Understanding Individuality

Ordinarily members of a species that reproduce sexually possess a paired set of chromosomes (diploid), in other words they are sexually dimorphic. In the mammalian female there is a homologous pair of 2x chromosomes (xx) while in the mammalian male there is an unequal pair (xy). What this dimorphism guarantees is that any population will be variable to the extent of two classes. When any particular behavior is encountered, whether the sex chromosomes or some other genotype differences are involved, remains a question for investigation separately for every population. But one thing is certain there is no room for dogmatic attitudes and assumptions about uniformity in a population such as the old behaviorists maintained.

Chromosomes other than 2x chromosomes are termed autosomes. Every autosome is normally represented by a homologous pair whose numbers have identical genetic loci. Alternative forms of a gene any of which may occupy a given locus are termed alleles. If an individual receives identical alleles from both parents at homologous loci, then he is said to be homologous for that gene, but if he receives two alleles that differ, then he is heterozygous for that gene. When a gene changes from one allelic form to another this process is termed mutation. When a gene is represented in the population pool by two allelic forms, then the individuals in this population will be variable, they will be either homozygous for the two alleles or heterozygous for their combination. Looked at this way, the organisms which we study are variable before they undergo varying environmental experiences. When we add individual experiences to the variety of genetic organization, it should be obvious to all why it is that individuals differ in behavior.

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The more reliable our methods of observation become, the more evident will this variety be.

If we look at behavior as the correlation of all systems in the body rather than the expression of any single one, then there is little reason to expect that the many possible combinations and integrations of these systems that go to make up the members of a population will yield homogenous responses to many behavioral measures of observation. We need only look at the various breeds of dogs and horses to expose the obviousness of these facts. For example, in laboratory experiments, some rats learn mazes more readily on the basis of visual cues, while others do better with predominantly kinesthetic cues.[1] In some domesticated rats, activity in the revolving drums were controlled by the gonads. Control rats had as high as 18,000 revolutions while gonadectomized rats scored only a few hundred. If the gonadectomized rats were given cortisone they regained a high activity level. When the same experiments were repeated on wild Norway rats, the presence of gonads made no difference in measured activity. They had larger adrenals to compensate for smaller gonads. So it appears that activity may be under the control of adrenal output in one case and gonadal output in another.

Study of populations has revealed that often extensive series of alleles exist for a locus. Well known examples are the at least three alleles for the ABO blood locus in man and a dozen or more alleles at the white eye locus in Drosophila.[1] These variations in series of alleles is further compounded by variations in architecture that can occur in a single gene. Benzer[2] in the T4 bacteriophage with a physical structure of about 2,000 nucleotide pairs found at least 339 sites for mutation.

Sexual reproduction involves meiosis which produces gamets having single chromosome sets. One set in our diploid complement is of paternal and the other of maternal origin. The assortment of segregating chromosomes in meiosis occurs independently for each pair. This process assure diversity because it ensures the likelihood that the gametes will receive unique hereditary endowment (genome). For example, gametogenesis in Drosophila produces eight alternative genomes from three chromosones. Man with twenty-three chromosome pairs produces gametes with any of two alternative genomes. It is clear why siblings cannot be genetically identical since the gametes contributed by each parent is chosen from two^{23} alternatives. The probability that the second offspring born to parents will have exactly the same genotype as their first born is one in over seventy trillion and the probability that two unrelated individuals will have the same genotype is zero. Assuming that there are 10,000 human genes and an average of four alleles for each gene, ten combinations per locus, we get the astronomical number of 10^{10000} potential human genotypes. It is obvious from all these calculations that every genotype is unique. This means that each individual's particular balance of physiological endowments will be the developmental result of the genotype he draws in the "lotteries of meiosis and the mating ritual."

L. H. N.

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2. Benzer, S., Proc. Nat. Acad. Sciences, V. 5, 47: 403, 1961.

The Dying Patient's Grief

> *Because the handling of the slowly dying and their families is so important, it is unfortunate that so rarely does anyone ever discuss the subject in medical schools, at medical meetings or in the journals.*—Walter Alvarez

There are ethical consideration in the treatment of the dying patient and this is excellently covered in a recent issue of the *Bulletin of the Charlotte Hungerford Hospital Medical Staff.*[1] It covers preserving life, deuthanasia, the dying and their treatment and care of the dying. Previously, the literature on the dying patient was primarily concerned with the fear of death and whether or not to tell a patient that he is dying. Generally strong opinions are held for or against telling the facts to the patient.

Telling is recommended because the patient has a right to know. He must be allowed to put his affairs in order. He will discover the truth anyway, or he will be a better person for knowing it! Not telling is supported because the idea of death is too much for a man to tolerate. He will tend to deny it anyway or the information may precipitate a suicidal depression. Both of these points of view assume that the most significant emotional problem of the dying patient is fear of death. If this were so then strength of personality, relative physical health, and conviction of a satisfactory after life should provide resources for the patient to face the experience philosophically. However, if the patient is depressed, is failing in health and is suffering, and if he lacks conviction of a satisfactory after life, then these should deprive the patient of such resources.

The fact is that a strong well-integrated personality has great difficulty to accept with equanimity the idea of his own death. Aldrich[2] describes such a person with friends, accomplishments and devout belief in a benign hereafter, who at first was profoundly depressed when informed that he had an incurable carcinoma. Later he managed to persuade himself that he was recovering in spite of evidence to the contrary. In this he was assisted by his friends who also used denial to perpetuate his belief. In short strength of personality may help a patient not so much to avoid depression in anticipation of death, but to engage in denial of the illness. On the other hand those who seem to accept death with equanimity have lost interest in living as a result of pain or intolerable disability. By leaving life they have really little to lose.

In dealing with such cases, the physician of course, has to distinguish between patients who face death with equanimity and those who are depressed or resort to denial. Apparently, Aldrich has not found that belief in a benign hereafter can account for the change in attitude in the direction of an increasing degree of acceptance of death instead of denial of death. To account for this, Aldrich turns to the concept of grief for an explanation.

The term grief is usually applied to the emotional experience of survivors at the loss of a friend or relative. It is a reaction to separation, whether for long periods without death or after death, and is not materially modified by belief in an after life. Schilder[3] suggested a process analogous to grief takes place in the dying person as well as in his relatives or friends. The dying person is also subject to interruption of interpersonal relationship but Eissler[4] believes it secondary in significance to the fear of death. However, if interruption of interpersonal relationships is so important in grief, it is easier to understand why the patient who is to lose both relatives and friends has more cause for grief or depression than the relative who does not lose all his friends but only one, the patient.

The more personality resources a person has the more friends he has to lose therefore the more grief and the more suffering. If we assume that interruption of object relations is the major threat of death, it can help to explain the greater acceptance of death often seen as death approaches. As the patient's illness continues, particularly when it is associated with pain, the patient is seen to become more concerned with himself and less concerned with outsiders. The significance of other individuals to the patient is gradually reduced and pari passu, the extent of the anticipated loss is reduced. In fact, the retraction of ego boundaries may continue to the point at which the patient no longer needs to deny or be depressed. At this point he can become more realistic and more capable of accepting death.

What then can the physician do to help his dying patient? First of all he needs to evaluate and reevaluate the strength of the patients personality, the status of his interpersonal relationships. This is necessary because patients vary in their responses to imminent death and even the responses of a specific patient may vary during the course of his disease. The physician also needs to understand his own attitudes towards death and the extent to which the death of a patient threatens his adequacy as a physician.

There is no arbitrary course applicable to all. Many of us may have irrational attitudes. Then there are limitations to our diagnostic ability and our right to make significant decisions for others. For these and other reasons it may be wisest to give the patient the opportunity to make his own choice. From the onset it must be possible to inform the patient of the serious nature of his illness and at the same time speak of the future in terms of both confidence as well as apprehension. In this way the patient is given the opportunity to select denial or acceptance according to his readiness at that particular time. He can choose then or later whether or not to face death.

Aldrich gives an excellent example of this approach. A surgeon has discovered an inoperable malignant lesion. On his first post-operative visit he proceeds as follows: Mr. X "as I knew you anticipated, we found a cancer. We did our best to remove all of it, but in situations of this kind we can never be absolutely sure, although we are optimistic about your future, you should nevertheless consider that there remains a possibility of a recurrence. You have had a good deal of surgical work done, and with the side effects of radiation we will have to give you for the fullest protection, you will need all your strength for some time to take care of your physical health."

The patient who needs to deny can believe the optimistic side of the surgeon's statement and can still put his affairs in order on the basis of prudence. He can take appropriate action and still reserve his own secret or open conviction that he is destined to survive. In fact he may even need to believe in his survival in order to put his affairs in order. Otherwise he might avoid taking steps if he believes they are propelling him in the direction of death. At the same time the situation is recognized as serious by patient, physician and family and so there is no need for anyone involved to act as if the illness were trivial.

The physician at the same time should continue to see the patient regularly and show continued concern about his future. This would contribute to the patient's conviction of potential survival and make unnecessary the patient's acceptance of death before he is ready to give up his defenses spontaneously. In short, the physician should not abandon, but continue his ministrations and com-

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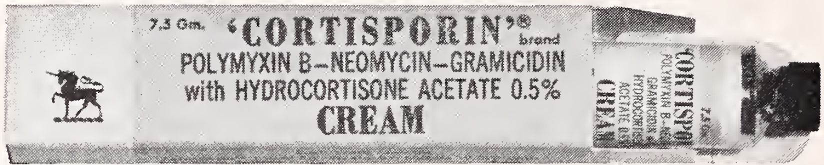
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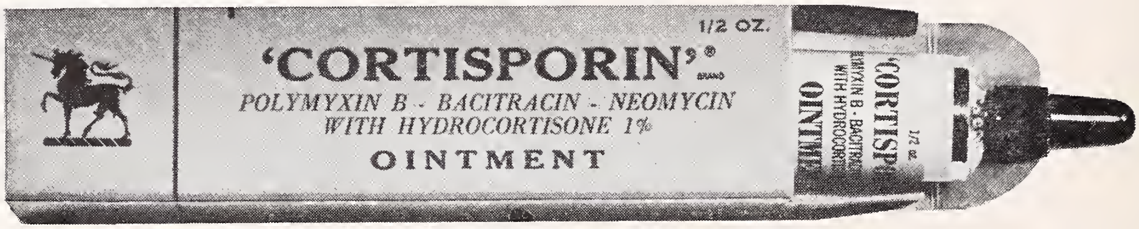

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Caution: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

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municate with the patient in terms that will permit him either to deny or accept death as his current emotional needs require. When the patient is still well and the separation grief may be great, he can use denial. When the suffering grows, and his absorption in himself increases, realistic acceptance of death will come automatically.

L.H.N.

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Physiology Of Sleep

Until ten years ago, it was believed that a "sleep center" existed in the central nervous system and that stimulation of this would cause a person to go to sleep. Actually, there is a small portion of the reticular formation located principally in the ventro-medial portion of the medulla which does have mainly inhibitory functions, since stimulation in this area causes greatly decreased tone of the musculature throughout the body. However, the problem is much more complicated since stimulation in various parts of the reticular formation can cause stimulation of some muscles and inhibition of their antagonists, and also cause marked activation of the cerebral cortex sufficient to cause a sleeping animal to awaken instantaneously. It would be expected that if the areas in the reticular formation which cause arousal and wakefulness were to be damaged either by brain tumor or hemorrhage or encephalitis, that then a person will pass into a state of coma and not be susceptible to normal awakening stimuli. It is thus apparent that wakefulness results from enhanced activity of the different parts of the brain, whereas sleep represents lack of adequate brain excitation.

The reticular activating system which is the relic of the primitive brain upon which the cortex has been superimposed, seems to have very little intrinsic activity. Instead it must be stimulated to action by sensory stimuli from both the body and higher brain centers. When an animal is asleep, the reticular activating system is in an almost totally dormant state. Yet almost any type of sensory signal can immediately activate the system. For instance proprioceptive signals from the muscles, pain impulses from the skin, visual signals from the eyes or auditory signals from the ears, can all cause sudden activation of the reticular activating system and therefore arouse the animal. In addition, the cerebral cortex can also stimulate this system and increase its activity. In short, activity in the reticular formation can be intensified by the cerebral cortex from above and by bodily stimulation from below. The highest degree of arousal activity seems to be derived from muscle signals and brain signals.

When a person has been awakened, he tends to remain awake at least for the time being. He can only go to sleep however, if the reticular activating system either becomes fatigued or less excitable so that it cannot respond to somatic and cerebral signals, or if somatic and cerebral signals so decline that they cannot stimulate a fatigued reticular activating system. Once the degree of excitability of the neurons has fallen to a critical level, this represents the state of sleep. Implicit in this hypothesis of sleep is the assumption of a rising and a falling degree of fatigue in the neurones of the reticular formation. It is as if there is a rhythm in the reticular activating system comparable to many other rhythms we find in biology. We become sleepy at a certain time of day or night perhaps because our rhythm has reached a certain downward phase. When our temperature is falling, we find it hard to remain awake. We seem to follow this cycle both by habit and repetition.

Reticular deactivation then is the major point in sleep. Whether there is also inhibitory effects of both descending and ascending impulses, the fact is that very slight changes in synaptic efficiency could suddenly get to the stage where many feedback circuits were below a return level so leading to a very great depression of activity of the reticular activating system. There is thus effected a dissociation between the anterior and the posterior part of the brain by what can be called a "physiological section." The posterior part of the brain is sleeping and the animal will present a behavioral sleep, while the anterior part of the brain is awake. If this were true, it would explain dreams, how mathematical problems are solved, and experimental solutions found during sleep. It would explain the extraordinary finding of Kety's that the oxygen consumption of the brain does not decline during sleep.

After the reticular activating system has been dormant for a period of time then the neuronal cells in it gradually regain their normal degree of excitability. Wakefulness however, still will not occur until some arousal signal will initiate its activity. Gradually the reticular activating system responds to more and more signals from above and below and the person passes from the state of sleep into the state of wakefulness. The greater the intensity of the signals from the sensory systems and the greater the intensity of signals from activated regions of the cerebral cortex, the greater would also be the degree of wakefulness.

The physiologic effects of sleep are best learned from the condition of a person during prolonged wakefulness. Such a person often suffers progressive malfunction of the mind as well as of behavioral activities of the nervous system. We are all familiar with an increased sluggishness of thought that occurs towards the end of a prolonged wakeful period. In addition, a person can become irritable and even psychotic following forced wakefulness for prolonged periods. It is therefore, a reasonable assumption that sleep has a very beneficial effect in restoring normal "balance" between the different parts of the central nervous system.

The cycle of enhanced and depressed nervous excitability that follows along with the cycle of wakefulness and sleep also has effects on the periphery of the body. There is usually enhanced sympathetic activity during wakefulness as well as enhanced numbers of impulses to the skeletal musculature to increase muscular tone. Conversely during sleep sympathetic activity decreases and the muscular tone becomes almost nil. The arterial blood pressure falls, the pulse rate decreases, the skin vessels dilate and the overall metabolic rate of the body falls by some 10-20 per cent.

Although normal sleep closely approximates the unconscious state, the dangers that threaten a person in the unconscious state such as pooling of blood in the periphery progressive pulmonary atelectasis and respiratory obstruction are avoided. This is so because the brain in a sleeping individual can receive and interpret peripheral stimuli whereas an unconscious person cannot. During normal sleep, pain or discomfort break through his somnolence, awaken him, and cause him to change to a more comfortable position. Few persons if any, remain motionless during sleep, the majority changing their body position often. This activity has a twofold purpose. One is to prevent pooling of blood in dependent portions of the body thereby benefitting the circulation. By changing position one improves muscle tone temporarily, thereby facilitating blood flow.

The second purpose served by changing position during sleep, is to benefit respiration. The splinting of the chest muscles that occurs with turning is always followed by a deep inspiration which opens up alveoli. In this manner the tendency for development of patchy areas of pulmonary atalectasis is counteracted.[2]

An additional protection to assure adequacy of ventilation during sleep is the prevention of respiratory obstruction. Few people sleep on their backs for more than short periods and when they do, the head is usually turned towards one side. Otherwise the lower jaw relaxes, the tongue falls against the posterior pharyngeal wall, partial obstruction of the airways occurs, and snoring results. Occasionally, a snorer will achieve complete airway obstruction, but the normal sleeper never succumbs to this, because his pCO2 rises to stimulate his respiratory center, his pO2 falls to stimulate his chemo-receptors and he "fights through" the obstruction by a change in his body position. It should be obvious that the safest body position for preserving the airway is the lateral position.

In sleeping man the protective respiratory reflexes are active. He is subject to arousal by ordinary stimuli. The olfactory nerves warn of offending odors, and tracheal reflexes react to the presence of foreign materials. The respiratory cilia, move secretions toward the bronchi and trachea where their presence precipitates coughing. In short the brain in a sleeping individual can receive and interpret peripheral stimuli. Pain or discomfort break through in somnolence, awaken him and cause him to change to a more comfortable position. When alcohol, drugs, or disease block the reception of the danger signals, then the physician must do for the unconscious patient, what he does for himself during sleep to avoid pooling of blood, prevention of pulmonary atalectasis and preservation of airway integrity. For the unconscious patient will have lost most if not all his normal protective devices and he must depend upon others to detect or anticipate his needs.

L.H.N.

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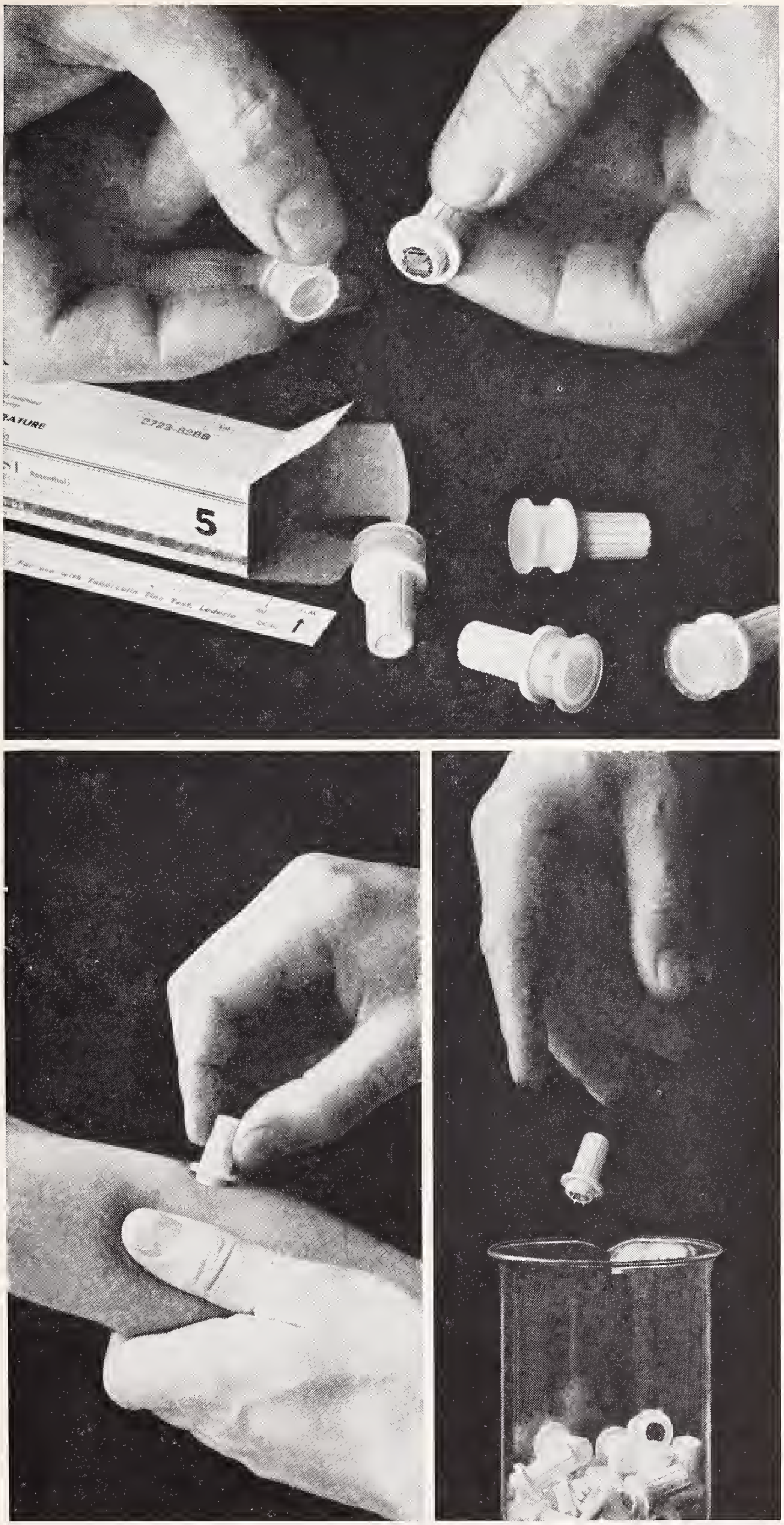
The Rational Physician And His Use Of Drugs

"To write prescriptions is easy but to come to an understanding is hard." Kafka in The Country Doctor.

DeHaen[1] has reported that 4,562 new products including 1,050 new dosage forms were marketed in the past ten years. To be sure some were duplicate products, some were compounded products. All had at least two names, a trade name and a public or non-proprietary name and most also had one or more chemical names. To glean information about these drugs the physician has access to four



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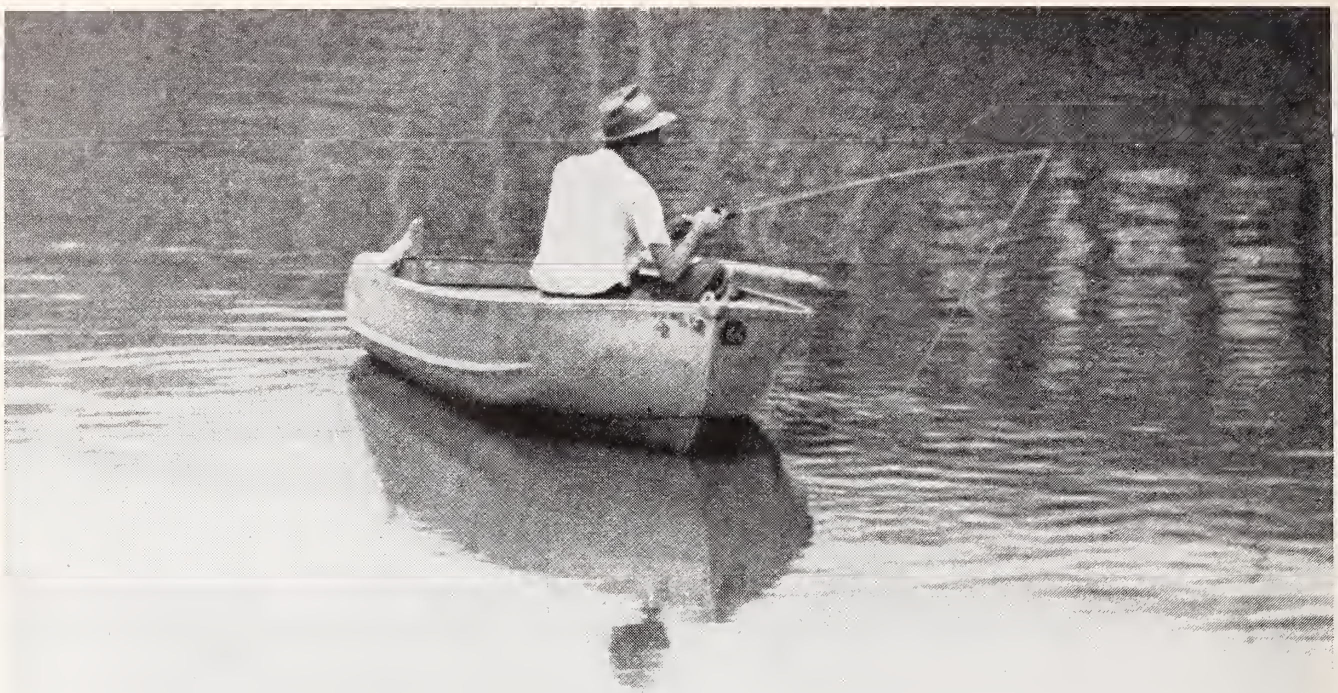

The discharged
mental patient . . .
and Thorazine®
brand of chlorpromazine

"The average practitioner is quite capable of handling the vast majority of ex-institutionalized patients by regulation of medication, reassurance, manipulation of the environment where necessary, and . . . other technics." Kline, N.S.: Postgrad. Med. 27:620 (May) 1960.

The family physician must often assume responsibility for the discharged mental patient. Thorazine (chlorpromazine, SK&F) can be a valuable adjunct to the continuing care of this patient, because it helps prevent relapses by insulating him from the impact of stressful experiences. For successful rehabilitation and prevention of rehospitalization, however, the former mental patient—and often his family—also needs the guidance and counsel of his physician.

Many physicians are surprised by the high doses of Thorazine (chlorpromazine, SK&F) used in patients released to their care from mental hospitals. This surprise may be expressed by a drastic reduction in dosage "to play it safe"—with serious consequences for the patient.

The successful maintenance of former mental patients requires adequate, often "high" dosage, and often for prolonged periods of time. Fortunately, these dosages do not mean greater risks for the patient. On the contrary, there is much less risk of serious side effects once a patient has become gradually accustomed to Thorazine (chlorpromazine, SK&F)—*regardless of dosage*—over a period of a few months. Continuing therapy is almost always well tolerated, and is essential to most patients' continued well-being.

Brief Summary: Thorazine (chlorpromazine, SK&F) has been successfully used for 10 years in the treatment of mental and emotional disturbances, and has proven highly effective in the maintenance therapy of former hospitalized mental patients. *Principal side effects:* The most frequently encountered side effect is transitory drowsiness. Other occasional side effects include: dry mouth, nasal congestion, constipation, miosis, dermatological reactions, photosensitivity, jaundice, hypotension, increased appetite and weight; very rarely, mydriasis, agranulocytosis, extrapyramidal symptoms. *Contraindications:* Comatose states or in the presence of excessive amounts of C.N.S. depressants.

For complete prescribing information, please see *PDR* or available literature.

SK&F *Smith Kline & French Laboratories*

hundred and forty medical journals published in the United States. He also obtains some information from meetings of medical societies and hospital staffs and from post graduate courses. But he also comes in contact with his colleagues, with detail men and sometimes with *Time* magazine. How does he handle this niagra of drugs poured upon him? It is literally poured upon the physician, for in the last analysis the responsibility for prescribing drugs rests upon him. It is he who must make the decision whether or not to use a new drug on a particular patient.

When physicians were questioned regarding a drug they had recently prescribed for the first time, forty-eight per cent stated they had learned about it from detail men, twenty per cent from direct advertising and eight per cent from other doctors.[2] In short, three quarters of physicians questioned were using drugs, knowledge of which came not from scientific publications or even from experts in their field but from advertising sources. Under such circumstances it is inevitable that the reasons these physicians were using new drugs were not sound ones and that the information they relied upon was biased information. It cannot be of too much help to the patient. It cannot lead to growth and understanding on the part of the doctor of the mechanism of the drug's action.

There is a tendency for some physicians to think that the latest is the best and that failure to use a new drug will stamp them as being behind the times. Indulging in a little historical perspective, can introduce an element of rationality for in another generation it can safely be predicted that less than ten per cent of the new drugs will remain in the United States pharmacopia if we are to judge by the experience of that last thirty-five years.[3] The average life expectancy of a male physician after he graduates from an American medical school is 44.7 years.[4] There will be hundreds of laboratory tests incorporating newly learned basic principles that will be devised during his lifetime and the present newest drugs will be forgotten for the most part. We obviously need to recognize the sound reasons that should motivate a physician in the use of a new drug.

The rational physician, by contrast with the one subject to subtle suggestion, decides to treat a patient on the basis of the disease the patient has, its pathophysiology, its natural history, the drugs that will combat the disease and how they work. The wise doctor, in those cases in which he does not fully understand the mechanism of the drugs action, nor how effective it has been when used in similar cases treated by others, will seek the advice of experts either through consultations or by reading what they recommend. In this way, he will gain understanding of what he is doing, he will gain the approval of his colleagues. This will encourage him to stay abreast of the latest knowledge concerning the human body and the drugs that act on it, to learn the latest findings on the heels of the investigators. But to learn of the latest findings without integrating these discoveries into his day by day practice is not enough. "Undue emphasis has been placed on the goal of 'bringing new information to the physician,' it is more important to help him cultivate his analytical ability and improve his critical judgment."[5]

This goal sounds elementary, but it is not so easy to achieve. Obviously, we need to restudy the means available for providing post-graduate education in the light of present day physicians needs. We must utilize our resources to make the physician as competent as possible, for this ideal has been set for us, as we are setting it for todays medical undergraduate.

One step towards creating the rational physician that should be taken, is to eliminate the superfluity of information, suggestions and misinformation that comes to the physician, or at least to make him conscious of the distinction between advertising and scientific truth. The responsible members of the medical profession do not approve of misleading and suggestive advertising and it is gradually being eliminated in media over which we have control, such as medical journals and exhibits at medical society meetings. This responsibility is keenly felt by editors, editorial boards and by the elected and appointed officials of medical societies. The practicing physicians collectively have the power, if they wish to use it, to eliminate advertising that they consider improper.

When the physician can recognize correct information from biased information, it would be a long step towards improving the prescribing of drugs. For then he will be able to explain to the patient what drugs he is prescribing and what he expects to accomplish with them. Such explanations will serve several useful purposes. They will make the doctor keener in his judgment. They will ensure more co-operation and better reporting from the patient of untoward reactions. They will protect the doctor if untoward reactions do occur. Equally important will be the confidence which the explanation will create in the patient towards his doctor.

L.H.N.

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The Placebo Phenomenon

In the final analysis any drug which has been tried out and found effective in an animal, must be tested upon man. But, when we come to use man as a test animal, another major problem confronts the clinical investigator, for we now have to take into account, certain unique attributes of man, memory, psychophysiology, reactivity, judgment, emotional and situational reactions, all of which can, and do modify responses to pharmacologic agents. This problem can best be appreciated by a consideration of the placebo phenomenon.

Physicians have used placebos since time immemorial. Before the era of modern therapeutics, probably most drugs and procedures that the physician employed with few exceptions depended upon their placebo effects. Strangely enough, prior to 1945, no reference to the placebo phenomenon could be found in the *Quarterly Cummulative Index Medicus*[1] although individual investigators have had recourse to the placebo frequently in studying efficacy of drugs upon man. Thus Diehl[2-4] utilized the placebo in evaluating various substances used in the treatment of the common cold. With the help of the placebo Diehl and his colleagues were able to show the lack of benefit derivable from multivitamins and from many of the commonly used cold remedies. Of the subjects who received saline placebos in the vaccine study, 7 per cent complained of untoward symptoms which they attributed to the vaccine! A small percentage of the subjects who received oral lactose placebos complained of "toxic" symptoms!

Similar experiences were reported by Wolf and Pinsky[5] incident to their study of mephenesin. They found several patients, who had received lactose as a placebo, complain of "complications" of considerable magnitude. And these authors report the striking experiences of Tucker who studied streptomycin.[6] Sixty-one per cent of the subjects in the placebo group experienced one or more of the commonly accepted complications of streptomycin therapy such as loss of high-tone and low-tone hearing, eosinophilia and impaired urea clearance! The unwary investigator or observer would suppose that lactose is the most effective drug for treating most of mankinds ills! Obviously, not all toxic reactions to pharmacologically active agents can be attributed to the drug.

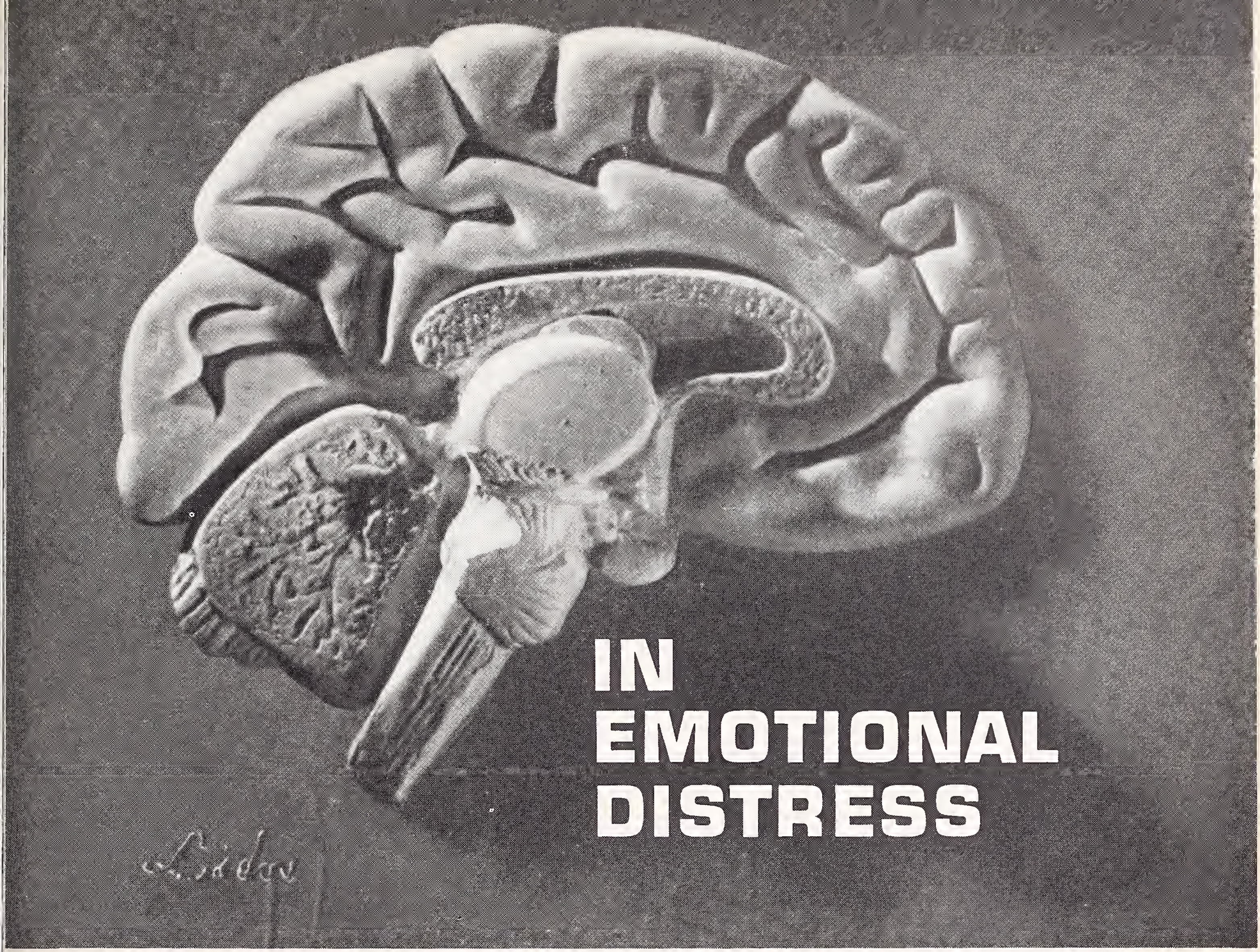
Lasagna[7] studied the placebo response extensively and found that the placebo may mimic the activity of many drugs. In patients with tuberculosis he was able to instill a feeling of "pep and energy" with placebo therapy and even demonstrated cumulative effects. In producing post delivery analgesia he found the response curves to aspirin or a placebo quite parallel. It is clear that placebo therapy must be recognized as capable of inducing cumulating effects and of paralleling pharmacologically active therapy, and also be a source of untoward or "toxic" reactions. It is obvious that such characteristics of the placebo makes the evaluation of any therapeutic agent in man extremely difficult.

Besides the "intrinsic" action of the placebo, a human being can actually be conditioned to respond to drugs in a special way. The way in which a drug is administered and the physiology status of the organ at the time of its administration can be important determinants affecting human response to therapy as Wolf has demonstrated in several studies.[8-9] In short, some humans can be characterized as "placebo responders." How can they be identified? What are their characteristics?

Lasagna's study of the placebo response to postoperative pain provides valuable information in this area.[10] The "nonreactors" seem to have experienced less post-operative discomfort and pain than the "reactors." They requested medications less frequently. They were more co-operative and more pleased with their medical care. The "reactors" suffered a higher incidence of dysmenorrhea and more somatic symptoms under stress. They could be characterized as more emotionally expressive. They had less formal education and attended church less frequently than the patients who did not react to placebo therapy. As a group, the reactors suffered more with their pain than the non-reactors,[11] who were emotionally more controlled than the "average" person of the same age and background.

Of considerable importance was the finding that there was a significant number of inconsistent responders. Lasagna attributed this in part to the variation in the intensity of pain that they experienced and in part to their pharmacologic sophistication which permitted them to distinguish between the active and inactive agent after repeated exposure to both drug and placebo.

These problems in the study of the influence of drugs in pain are well exemplified in the case of studying effects of drugs on patients with angina



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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

pectoris. For here improper study and premature use of new drugs could lead to the displacement of "older" agents of established efficacy by relatively ineffective compounds. We must certainly be aware of the vagaries of human response to treatment and at the same time encourage further investigations along the important lines of quantifying the effects of drugs in man.[11] An important part of all such investigations should be to eliminate from the study those that exhibit the placebo phenomenon.

L.H.N.

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Postgraduate Nutrition Education

Nutrition is integral to the total management of the patient, yet the practicing physician has not availed himself of the vast amount of knowledge on nutrition in his daily practice. There are many reasons for this. The chief one is the lack of planned and properly coordinated education in clinical nutrition in medical schools.

"Some of the basic concepts of nutrition are presented in the various preclinical departments of the medical schools, such as biochemistry and physiology," the Conference on Nutrition Teaching in Medical Schools found.

"In the clinical departments and subspecialties of medicine there has been insufficient correlation of the subject matter, so that the student does not have a precise grasp of the fundamentals of nutrition and is, therefore, not able to apply modern nutritional concepts."

To fill the void in the area of postgraduate education in clinical nutrition, the Philadelphia County Medical Society and the State Society five years ago initiated a grass-roots nutrition education program among physicians in Pennsylvania and surrounding areas.

Methods

A panel of more than fifty nationally known physicians who are also oriented in the basic and clinical phases of nutrition was recruited to fulfill speaking engagements. This provided an opportunity for experienced clinicians to exchange with practicing physicians information on the newer concepts of nutrition as applied to the total care of the patient.

To implement the program various means have been utilized, such as individual lectures, symposia, panel discussions, a one-day institute of nutrition, and presentation of discussions on nutrition at regularly scheduled hospital staff meetings. Other organizations, such as chapters of the American Academy of General Practice, state and county medical societies, food and nutrition councils, and county dental societies also cooperated.

In addition to formal lectures on nutrition, detailed discussions during ward rounds of individual patients presenting nutritional problems were utilized to emphasize the responsibility of the physician for dietary treatment together with close observation of the patient's nutritional deficits and response to the nutritional therapy ordered.

Topics

Since nutrition permeates every field of medicine, a large variety of specific medical and dental problems of current concern to the practitioner have been offered; e.g., obesity, cardiovascular disease, gastrointestinal disorders, diabetes, mellitus, alcoholism, hematological disorders, surgery, nutritional problems of pregnancy, infancy, adolescence, and aging.

Acceptance

The Nutrition Education Program has been well received by the profession and several medical organizations have requested repeat nutrition programs.

Michael G. Wohl, M.D., *Chairman*
Committee on Nutrition and
Metabolism, Philadelphia County
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The relatively few conditions in which Lomotil has given less than satisfactory control have been, for the most part, those such as severe ulcerative colitis in which too little anatomic or functional capacity of the intestines remains for the motility-lowering action of Lomotil to have effect.

It should be noted, however, that Lomotil has proved highly useful in mild to moderate ulcerative colitis and in several other refractory forms of diarrhea.

The recommended initial adult dosage is two tablets (2.5 mg. each) three or four times daily, reduced to meet the requirements of each patient as soon as the diarrhea is controlled. Maintenance dosage may be as low as two tablets daily. *Children's* daily dosage (in divided doses) varies from 3 mg. for a child of 3 to 6 months to 10 mg. for one 8 to 12 years of age. Lomotil is an exempt narcotic; its abuse liability is low and comparable to that of codeine. Recommended dosages should not be exceeded. Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia. Lomotil should be used with caution in patients with impaired liver function and in patients taking addicting drugs or barbiturates. Lomotil is a brand of diphenoxylate hydrochloride with atropine sulfate; the subtherapeutic amount of atropine is added to discourage deliberate overdosage.

Research in the Service of Medicine SEARLE

IV. Diagnosis And Therapy

A. Diagnosis Of Radiation Damage

Marshall Brucer, M.D.

■ Talking about radiation damage is like talking about "diarrhea" or "infections"; these can range from a minor inconvenience to a rapidly lethal event. For the purposes of discussing diagnosis we shall assume the following:

Low-dose or incidental disease. If less than 100 r exposure, the patient will probably manifest, if anything, only incidental disease during the first two months following an alleged accident.

Medium-dose or possibly severe disease. If the patient has been exposed to between 100 and 1,000 r there is a good possibility of an acute radiation syndrome. At 100 r the probability is that the disease will be minor; at 1,000 r the probability is that the disease will be lethal.

High-dose or probably lethal exposure. In this range the physician probably can do nothing more than express humanitarian concern and give terminal care.

We are concerned here only with the first 60 days following an accident, but in all incidents there are legal and public relations problems that might change an incident into a serious event.

History Of Accident

It is assumed that the physician will take a standard medical history as with any other patient. Pre-existing psychoneuroses, tumors (especially visible ones), sterility problems, visual defects and noticeable fatigue are especially important in the low-dose patient; it is advisable to have a medical history from relatives and friends as well.

Previously existing debilitating diseases can affect the patient's response to the dose of radiation he has received. A history of pre-existing infection, blood dyscrasia and visual defects is especially important in the medium-dose range.

In the high-dose patient there might be little time for a detailed history. Bowel function and water imbalance are items of special interest.

The patient's own story of the accident, with such details as exactly where he was in relation to the accident, exact time sequence and what he was doing, may be the only good health physics reconstruction. Health physicists, administrators and especially public relations people are prone to accept whatever parts of a patient's story fit preconceived notions about radiation. Therefore, an assessment of the possible validity of a patient's history is important. Since there is no time for base line studies, the history should include the availability of previous medical records. The patient's reproductive and sexual history should be in detail, especially in the low- and medium-dose patients.

Physical Examination

It is assumed that every physician will do a thorough physical examination as he would for any patient. Special description should be made of any trauma. Especially evidence of any minor infection and a description of the nails, the eyes and the hair should be detailed. A patient's statement as to what he feels "because of the accident" as for example, in the description of tumors, bruises and body temperature might be more important than the actual signs of a disease process.

Laboratory Examination

Little is known as to what laboratory examinations are necessary. Anything might or might not be of value. For example, a detailed examination of the blood-clotting mechanism was expected to be enormously important in one series of examinations; it was of little significance. (This was true in one series of patients; it is not necessarily true in the next accident.) Blood counts will show some effect and should be a matter of routine. It is probably best to follow standard operating procedures. If it is possible to do so without compromising the patient, a sample of about 20 cc of blood should be withdrawn, 10 cc frozen and stored for further tests if they are required. The first 24-hour and probably other samples of urine should be collected and an aliquot frozen and stored along with the blood sample. It is good practice to save, freeze and store any sample from any patient involved in a radiation accident. Even such things as the clothing, hair, or nail clippings should be wrapped separately and stored, at least until the investigation of the accident has been completed.

Contamination—Noncontamination

Even before the patient enters the dispensary or hospital it should be known that he is either contaminated or noncontaminated. If contaminated, it will be necessary to isolate the patient, all his clothing and everything his skin or clothing touches. Old sheets or newspapers are good enough drop cloths. Hospital personnel should wear rubber gloves and complete scrub suits when handling contaminated patients. The hospital personnel should be monitored after they take a bath unless positively known to be not contaminated.

Even if there is no history of contamination, it should be assumed that there is contamination until proved otherwise. Patients who have been exposed to neutrons (certainly), high-energy particles (probably), and very-high-energy electromagnetic radiation (possibly) might show some induced radioactivity. This is not contamination and cannot be removed by decontamination procedures. For example, the person who has been exposed to slow neutrons will have some of the Na^{23} of his body transmutted to Na^{24}. Such a patient is a high-background source of radiation and will be a hazard to any counting instrument. When the neutron dose has been low, such patients are not hazardous to other personnel; with a lethal neutron exposure, patients may be a radioactive hazard to medical personnel. When there is doubt, the patient should be isolated (time, distance, or shielding) until a measurement is made.

To Detect Contamination

A rough estimate of contamination can be made in any hospital radiology department, private medical or dental office with dark room facilities, or even by somebody who has and can develop photographic film. An unexposed film is wrapped in dark paper and is placed near the body for a few minutes, then it is developed. A control film should be wrapped in the same dark paper and put into the light for the same length of time as the unexposed film. If the exposed film is dark and the unexposed film is light, then the patient is emitting radiation. It takes further study to distinguish whether this is contamination or induced activity. A radiologist with good equipment can semiquantitate such film exposures. Any kind of an ionization chamber, pocket chamber, or personnel radiation monitor can give a semiquantitative distinction between large and small doses.

Some kind of a beta-gamma survey meter is an essential item where radioisotopes are commonly used. Not only can such a machine detect and distinguish between beta and gamma radiation, but it usually gives a reasonably semiquantitative result. (It will not detect alpha radiation.) The probe of the beta-gamma survey meter should be passed over the entire body about one-quarter inch from the skin at a rate of about one foot per three seconds. If activity is found, the area should be outlined by passing the probe over the area at a rate of about one inch per second. With some instruments, too high a reading can "freeze" the machine. This is easily corrected by scanning at a greater distance from the surface of the skin.

Once there has been a rapid hand scanning, if an instrument is available, the patient should be put into a whole-body counter to quantitate the amount of activity. If spectrometry is available and the history of the accident does not give evidence, the isotope responsible for the contamination should be determined.

Following a whole-body count, the patient should be put through a series of scans, depending on which instruments are available. A linear scan should cover the entire body from the hair past the toenails. An area scan should be used to accurately delineate areas of activity. These should be marked on the skin. A probe scanner, which measures only one point at a time, is usually a surgical instrument.

The proper personnel using the proper instruments can give an accurate localization of a reasonable amount of any radioisotope (with a few exceptions) any place in or on the body. One of the standard methods of detecting contamination is with a wipe test. The suspected area of contamination is wiped with a handkerchief and the handkerchief placed next to a piece of unexposed film or wrapped around any counting instrument. This can be a "quick and dirty" procedure or it can be done with great precision.

Blood

One of the first laboratory procedures will be to do a white cell count. The simple finger or ear-lobe puncture is sufficient. If arm blood is used, a platelet count and a differential white-cell count may be valuable base line data.

An ideal situation would be to take one blood count every hour for four hours, then every four hours for 24 hours, then every 12 hours for 96 hours, then daily for two weeks, then weekly for two months, and then monthly for six months, then yearly until the case is closed. Such an ideal procedure is not always desirable when the patient is seriously ill or has not been injured. Excessive laboratory work may cause an iatrogenic hysteria.

Blood Chemistry

Many chemical examinations of blood have been suggested. Most are worthless for diagnostic purposes; a few have been valuable but only as research information for an understanding of radiation effects. The initial definitive report in 1952 by Hempelman, *et al.* stated that there was a high urinary level of amino acids. For this reason both urinary and blood amino acid levels have been investigated. One part of blood chemistry does seem to have some significance. Creatine is snythesized in the liver, then transported to muscle, where it is converted to creatine phosphate. Much of the creatine phosphate is converted to creatinine before excretion but some creatine is also excreted in the urine. Following irradiation, there seems to be an excess of creatine in urine due to inability of irradiated muscle to utilize creatine. Along with creatinuria there is an increase in the excretion of betaaminoisobutyric acid (BAIBA). The BAIBA excretion appears to be roughly related to dose and to increase for only a few days and then it returns to almost normal levels. The creatine excretion appears to last for a number of weeks and is more closely related to dose (but still within very wide limits of variation). A survey of all the alpha amino acids excreted in the urine indicates that the excretion of taurine is very roughly related to dose but is not as specific to radiation as BAIBA nor does the increase last as long as does creatine.

There are as yet no good biological indicators of radiation damage that can be used in diagnosis or prognosis.

Bone Marrow

The study of bone marrow was important in hematology even before it was known that aplasia followed severe radiation exposure by a week or so. Bone marrow became extremely important when it was found that the protection of even a small portion allowed recovery from an acute radiation syndrome. It became an immediate therapeutic necessity when it was found that bone marrow could be transplanted from one family of rodents to another family within rather wide limits.

The study of bone marrow lost much of its importance in the field of radiation when the problems of a "secondary disease" were discovered. The secondary disease is presumably an immune reaction against a bone marrow transplant. The study of immune reactions has taken the place of bone marrow transplantation for therapeusis. There is as yet no evidence of a permanent graft of foreign bone marrow in a human being exposed to radiation; there is some evidence of a temporary graft. There is considerable evidence of successful grafts in identical twins

Diagnostically, bone marrow aplasia is an almost quantitative indication of the degree of radiation damage that has occurred within the medium range of human exposure. The far more easily demonstrated leukopenia and thrombocytopenia on peripheral blood give almost as much diagnostic and prognostic information.

Training The Doctor Of Tomorrow

In matters of health and medical care, the doctor no longer stands alone. He continues to be the leader and captain of the team, or teams, but he is assisted by at least 132 groups who have been specially trained in careers of health service. There are in the United States 2,500,000 people engaged in the so-called health professions. Today, doctors do many things. There are thousands of doctors who are never seen at a patient's bedside. Dr. A. travels to the hospital administrator's office or to the Dean's office with a brief case; Dr. B. spends his working life amid test tubes; Dr. C. is a detective who can tell whether a woman was hanged or strangled; and Dr. D. tests whether atom scientists have absorbed excessive radiation. Thus, I could go on and on, down the alphabet several times. The doctors who treat patients, however, whether in their offices or at the bedside, are the men responsible for the doctor-patient relationships and are largely responsible for the public attitudes about the profession.—Chester S. Keefer, M.D. *Training the Doctor of Tomorrow,* Boston, The Boston Medical Quarterly, 12: 87, 1961.

IV. Diagnosis And Therapy

B. The Treatment Of Acute Radiation Damage

Marshall Brucer, M.D.

There is no specific therapy for acute radiation damage. Therapeutic vitamins, ACTH, biologicals and antibiologicals all have been recommended. Beyond Madison Avenue, they have no value. Some of the symptomatic treatment, though not specific, appears to be of value. It is assumed that every physician will maintain the nutritional status of any patient. The psychological problems affecting patients following an accident are probably important. In accidents there is always a radiation hysteria with understandable concern by family and friends. The psychological problem may extend beyond the patient; there may also be administrative and public relations hysteria. There has been direct commercialization of the accident in the past. There may be demands for specific therapy by experts who have never treated patients. In the past these demands have ranged from the immediate injection of fetal bone marrow (Oak Ridge, 1958) to out-and-out quackery. Sometimes it is difficult to separate the administrators from the witch doctors. It is *not* assumed that the physician will handle this adequately but it *is* assumed that he will have to handle it anyway.

In the low range of radiation dose (less than 100 rads) probably no therapy is desirable other than reassurance to the person involved. In the high range (greater than 1000 rads) probably nothing effective can be done; the only logical procedure is to make the patient comfortable, to treat vigorously every symptom that appears, and to use any and every experimental procedure that might be indicated. At the upper end of the middle range the symptoms may develop rapidly and many therapeutic procedures will probably be done too late unless anticipated (admittedly this is eyebrow-lifting radical).

It is in the dose range of around 100 to 1000 rads that medical therapy can be of necessary value. In the light of the large amount of publicity on the small amount of work being done in experimental therapy, there will probably be demands for the physician to attempt procedures that might be more dangerous than the radiation itself. Most patients who absorb less than about 500 rads are not in a real life and death danger from the radiation itself. Their danger is from the complications of the radiation accident. Some of these complications are treatable. The physician should tend to be somewhat more conservative when the dose is less than 500 rads. When the dose is more than 500 rads the entire picture is more rapid and more severe, and the therapy should probably tend to be somewhat more radical.

Decontamination

First get rid of anything that might increase the radiation dose. In an electromagnetic radiation exposure, the damage is done before the physician sees the patient and nothing can reverse it. In contamination accidents, it is necessary to institute decontamination procedures early. These are simple and easily applied. Warm water and soap are sufficient to remove most contamination. If there is still activity, then a mild scrubbing, especially in the folds of the skin is necessary; if there is still contamination, then a more severe scrubbing localized to where the contamination is. The application of chelating agents has usually been unsuccessful but might, depending upon the isotope, be of value. Where the contamination is imbedded under the skin surgical removal is necessary; the surgeon consulting with a knowledgeable health physicist must weigh the risks of a slower metabolic elimination with a faster surgical removal.

Most of the common biological elements, H^3, C^{14}, Na^{24}, Cl^{36}, have a relatively short (a couple of weeks) half-time in the body. A few hundred microcuries are well within an acceptable range. Some of the nonbiological elements, Ra^{226}, Th^{234}, Pu^{239}, have a long half-time in the body (centuries) and only a minute amount (less than a microcurie) is a significant additional exposure. Even rather severe surgical removal is probably less risky than leaving in an appreciable amount of plutonium. However, leaving much tritium in the body is probably less severe than even the most simple surgery.

If there has been a neutron exposure, there will probably be a sodium and a potassium activation which may be confused with contamination. Both radiosodium and radiopotassium so induced have about a half day's half-life and the activity will disappear no matter what has or has not been applied to the patient. Until we have better methods of complete exsanguination and resanguination no therapy is either possible or desirable for the induced radioactivity.

Medical Therapy

During the first few hours following an accident the patient should probably be admitted to the hospital at an exposure of about 250 r. The physician should realize that establishing a 250 r exposure can seldom be more than a poor estimate during the first few hours. Where bed space is available we recommend hospitalization at about 100 rads. Where bed space is at a premium then hospitalization at about 250 rads is recommended. Sedation is indicated even with low exposures. This sedation may be mild and conservative at very low doses and become more vigorous as the dose estimate increases or as the appearance of the patient indicates.

Even in very low exposures there might be some purely psychological vomiting. It is probably better treated with sedation than with antiemetics. If, however, the vomiting is severe, looks as though it will be prolonged, and certainly where there is an estimate of high dose, it is valuable to give antiemetics even as a prophylactic procedure. But probably the most important therapeutic procedure that can be performed during the first few hours is to resist the temptation to load the patient with blood, drugs and synthetic metabolic poisons.

During the first few days (after the initial confusion has passed) it should be possible to distinguish the very high-dose patient from the very low-dose patient. The indicated therapy at this time is bed rest and sedation. During this period there should be enough indication from the pattern of vomiting that antiemetics are either indicated or not. It should be apparent from the fluid balance of the patient whether electrolytes should or should not be given.

It might not be apparent from the temperature charts that the patient has an impending infection. Antibiotics are not indicated in very early fever. With an early estimate of low dose, the physician probably should not give antibiotics during the first few days. Especially with indication of high dose the use of antibiotics is merely an added burden to the metabolism of the patient. Blood at this point is not only unnecessary, but is undesirable.

Bone Marrow

After the first few days, the question of bone marrow grafts should be considered. It was once thought that bone marrow replacement was valuable. Now it is thought to be somewhat useless except where an identical twin is the donor. Bone marrow replacement might be valauble in some diseases, and in the therapeutic irradiation of leukemias. There is some evidence that donor bone marrow, even though not a permanent graft, will assist the patient during the most severe phase of radiation disease. The evidence, either way, is not good and bone marrow replacement should be considered radical therapy.

Infection

During the period of greatest pancytopenia, a few weeks following the accident, there seems to be an increased predilection towards infections of all kinds. It has even been suggested that irradiated patients should be kept in an almost totally sterile environment. There is no good evidence that this is successful, but then neither is there any evidence that it is unsuccessful. During the period of developing infection the use of antibiotics is desirable.

Fatigue

Toward the end of the first few days many patients in the medium-dose group will appear to get better. There will be a temptation to let him out of the hospital. Experience has shown that all these patients will have alternating waves of well-being and fatigue. This is probably a very real symptom indicative of pathologic changes.

Bleeding

During the second or third week after an exposure, the total neutrophil count will be declining steadily and the platelet count will indicate a probable onset of hemorrhagic complications. Rest and sedation are still indicated. The platelet count will indicate the necessity for preparing for blood transfusion. There is considerable evidence to indicate that fresh, whole blood is decidedly superior to bank blood. It should be remembered in giving fresh, whole blood that in part this is a replacement of destroyed platelets, but that platelets are only a part of the clotting mechanism. Since some of the bleeding tendency is due to increased capillary permeability, overloading a patient with blood might be just as damaging as not giving any blood. The prophylactic use of "platelet-enriched plasma," if available, is indicated during the periods before actual bleeding. The use of fresh, whole blood adds more than just platelets and may be even more desirable after bleeding has occurred. A conservative rule to follow during the first few weeks following an exposure is that there should be a plain and unmistakable indication for anything that is injected into the body.

Summary

Decontamination, if indicated, is a primary concern in treatment. Sedation and bed rest are probably of value throughout the course of radiation disease. Antinauseants, antiemetics, antihemorrhagics and antibiotics are probably of value when they are specifically indicated. There is no indication that ACTH, or any drug, is of any value. Intensive vitamin therapy is a highly commercialized waste of effort. There is considerable doubt that bone marrow replacement is of any value. There is doubtful evidence that taking relatively severe sterility precautions does have some value. It is questionable that antihemorrhagics are of any value, but platelet-enriched transfusions and use of fresh, whole blood are probably of lifesaving value when they are indicated by hematologic laboratory work that is available in every hospital.

Principles Of Research

In the temple of Science are many mansions, and various indeed are they that dwell therein and the motives that have led them thither. Many take to science out of a joyful sense of superior intellectual power; science is their own special sport to which they look for vivid experience and the satisfaction of ambition; many others are to be found in the temple who have offered the products of their brains on this altar for purely utilitarian purposes. Were an angel of the Lord to come and drive all the people belonging to these two categories out of the temple, it would be noticeably emptier, but there would still be some men, of both present and past times left inside. . . .

Now let us have another look at those who have found favor with the angel. Most of them are somewhat odd, uncommunicative, solitary fellows, really less like each other, in spite of these common characteristics, than the hosts of the rejected. What has brought them to the temple? That is a difficult question and no single answer will cover it. . . .

A finely tempered nature longs to escape from personal life into the world of objective perception and thought; this desire may be compared with the townsman's irresistible longing to escape from his noisy, cramped surroundings into the silence of high mountains, where the eye ranges freely through the still, pure air and fondly traces out the restful contours apparently built for eternity. With this negative motive there goes a personal one. Man tries to make for himself in the fashion that suits him best a simplified and intelligible picture of the world; he then tries to some extent to substitute this cosmos of his for the world of experience, and thus to overcome it. This is what the painter, the poet, the speculative philosopher and the natural scientist do, each in his own fashion. He makes this cosmos and its construction the pivot of his emotional life, in order to find in this way the peace and security which he cannot find in the narrow whirlpool of personal experience.—Albert Einstein. *Essays in Science.* New York, Philosophical Library, Inc., 1934, pp. 1-3.

IV. Diagnosis And Therapy

C. The Chronic Radiation Chronic Syndrome

Marshall Brucer, M.D.

■ Beyond stating the problem and much clever work on postaccident calculation of radiation dose, there hasn't been much thought put into the treatment of chronic radiation damage. The general answer by standard documents to questions about treatment is "send the patient to the nearest doctor." I'm not sure what the nearest doctor does, but I think the best advice is for him to send the patient to the next nearest doctor. From the way things have been handled probably the best advice is to send the next of kin to the nearest private lawyer to start proceedings against the government. This at least, is almost certainly successful.

Chronic is a long time. When we say *acute* radiation, we usually mean that the radiation exposure has been completed in less than hours. An exception is external contamination which is dealt with elsewhere. Internal contamination is not so easy to deal with. As yet there have been no examples of accidents involving *internal contamination* that had to be *removed immediately* resulting in *chronic damage*. There have been a few examples of explosions during chemical preparation of fission products or reactor materials, but these were handled very quickly. They are a kind of acute treatment of what might possibly have been chronic radiation damage. The pre-World War II (thoroughly legitimate then) medical use of thorotrast and radium injections might be considered as chronic radiation accidents, but little besides obvious care was done therapeutically.

The treatment of the *chronic results* of *acute radiation exposure* is similarly shrouded in a haze of grantmanship, but it is a separate topic and should be discussed. There are some good (historically) examples of chronic exposure to the early radiologists. Most of these occurred and were treated during the early days of the X-ray. The treatment, however, would still be the same: amputation for malignancies, plastic surgery for "burns," symptomatic palliation where no surgery is possible. Since there is nothing new to discuss concerning the radiation treatments, it will be dropped from further consideration (but it can't be dismissed this easily from medical concern).

Internal Contamination

There are a large number of radioisotopes, an even larger number of chemical compounds, and many routes of admission to the body. Each of these might have a different pharmacology, not even the best pharmacologist could describe each of the possible conditions. Further, many of the possible contaminants are of elements and compounds unusual to the pharmacologist. Therefore, we have to make generalizations which admittedly are based largely upon ignorance.

The first principle of treatment of internal contamination (this is also the last principle) is "get rid of it!" The two big questions are, "How much" and "How?" The "How much" question is not too difficult provided you do not approach the essential question of "How much is too much?" I have a tabular description of a relative physical dose for 276 radioisotopes, but this includes only those that might have some medical usefulness in radioisotope diagnosis and therapy. It does not include alpha emitters or some very long or very short half-life materials which might be of great importance in accidents. There are whole books published on the problems of calculating dose. Given a few basic assumptions it is possible to arrive at reasonable estimates. Most of the national and international radiation safety councils have published detailed information on "maximum permissible dose" or "radiation protection guides," but these usually refer to either large populations or 100 per cent safety or "almost certainly no effect" or "what you should design toward." They do not assist the physician in balancing the risk of therapy with the risk of radiation decontamination.

A rule of thumb to follow (but this is only a rule of thumb and is neither definitive, nor authoritative, nor backed up by experience) is that when the radiation reading is ten times the background (for the particular machine used to make the reading), it is probably worth considerable medical risk to reduce the internal contamination. This is particularly true for chemicals known to be toxic; it is probably not true for chemicals known not to be toxic. It is particularly true for radioactive materials known to have a long half-time in the body; it is probably far too stringent a requirement for chemicals known to have a short half-time in the body. Where the radiation reading is less than ten times the background (of the machine being used), therapy to remove the contamination is probably only worth a minor medical risk. Such a statement is subject to the same hedges that are applied to the over-ten-times-background rule.

After a diagnosis of "How much" is made, the question becomes "How to get rid of the contamination" (if it is decided that it is necessary to get rid of it). Surgical removal is obviously best if it can be done in a hurry without much risk and without unnecessary deformity. Medical removal is more difficult for ingested materials; obviously emetics, purges and enemas are indicated. Emetics are valuable only in the first few minutes. Purges are valuable only with the first few hours and enemas are valuable only when there is definitely some activity in the feces.

The problem of determining a time at which a procedure is or is not valuable is a little bit more difficult than would seem at first. For example, if a non-absorbable substance is swallowed it can cause a denudation of the gut wall. Usually this is in the large bowel and purges may be valuable even after many hours. Even for absorbable materials there may be reabsorption into the gut, and purges or enemas may be valuable even after days.

There has been a lot of talk about the use of various chelating agents. Usually these are valuable early after absorption and while the material is still in the blood stream. Depending upon the compound ingested, they become less valuable as time goes on. For example, calcium in the process of transport is well chelated and excreted. Once it is bound into the matrix of bone it is poorly chelated and poorly excreted. It is a good but rough generalization to say that chelating agents are good only while the material is either in the blood stream or very lightly bound to "permanent" structures of the body.

Many years ago it was found that giving the body a large amount of stable iodine would block the thyroid gland from picking up a later injection of a smaller (chemical) amount of radioiodine. Later studies in animals found that the same "blocking" action would occur by pure dilution if large amounts of a stable element were given before administration of a much smaller (chemical) amount of the same radioactive material. But this was never so specific as in radioiodine. Stemming from this, there has been considerable newspaper talk about "flushing the body" with stable isotopes of the same element in order to remove radioactive contamination. This might be a good procedure if you could give the material immediately *before* the accident occurs. But you must be sure that the stable element is not more toxic than its radioactive isotope. Such a procedure, in the absence of anything better, might be worth trying postaccident provided all the requirements of good therapy are met.

Along the same lines, the use of various artificial-kidney type preparations has been suggested. It is probably possible to remove almost any chemical compound selectively if it is in the blood stream and if you know what the chemical compound is. I don't know that such a procedure has ever been tried in an internal contamination accident.

Diagnosis And Therapy Of Chronic Radiation Damage

Over and above the removal of continuously contaminating radioactive materials inside the body, is the problem of the treatment of the chronic effects of the radiation. This is treated symptomatically just as in acute radiation damage.

The chronic effects are usually described as cancers, leukemias, shortening of the lifespan, genetic abnormalities and birth defects. The treatment of cancers and leukemias, if (I said "if" and not "when") they are caused by radiation, is the same as the treatment of the same disease induced by any other cause. The problem of shortening of lifespan cannot be determined in any single patient. It can only be determined in large populations with large exposures. There is just as much evidence that there is an increased lifespan following low dose as there is evidence showing a decreased lifespan following large dose. None of this evidence is very good. Besides, there is no therapy even if it were possible to predict a decreased lifespan.

Cataracts should be mentioned. They are unusual events usually following an acute exposure rather than a chronic exposure; I have never heard of a cataract being implicated with a chronic exposure to radiation. Whether or not a cataract can be related to a radiation event, it is a slowly developing disease that is best referred to an ophthalmologist for definitive therapy.

Genetic Defects

During the years 1948-1954 virtually all births (over 70,000) in Hiroshima and Nagasaki were recorded. Six thousand were from parents one or both of whom had received atomic bomb exposure within 2000 meters. No evidence of major genetic damage was detected. The incidence of stillbirth, overt congenital abnormalities and neonatal mortality was not increased in offspring of the irradiated parents. It was clear from the study of the Atom Bomb Casuality Commission that "genetic damage was of little clinical consequence."[1]

Effects On Children Exposed *in utero*

The only good evidence of exposure of humans *in utero* are from the Japanese atomic bombs. There were frequent abortions and stillbirths in pregnant women, hence, less than 1000 exposure births occurred. Thirty-three Hiroshima children were found to have microcephaly. There were 15 mentally defective children. It appears that a very high radiation dose to the fetus during early gestation usually produces central nervous system disease. There is no specific therapy (related to the radiation) that can be applied to the children. It would appear that a sublethal total-body radiation dose to a mother during the first semester of pregnancy is an indication for a therapeutic abortion. The usual therapeutic procedures for the acute radiation syndrome apply to the mother. There is no therapy for the fetus. There is no evidence that a lower dose will produce the same defects or an even lower incidence of the same defects. There is a rationale for making extrapolations to lower dose in cytogenetics studies based upon a "linearity hypothesis" (whether believed or not). Neither a linearity nor a threshold hypothesis is appliacble in developmental defects.

Reference

1. Hollingsworth, J. W., Beebe, G. W., Ishida, M., and Brill, A. B.: Seminar Proceedings, 5 September 1960, A/AC 82/Seminar, United Nations, New York, 1962, pp. 77-100.

Doctor And Patient

The relation of doctor and patient, from which medical science and practice arise, conditions everything within the field of medicine and is itself conditioned by the nature of human relations in general. The patient is a person who is anxious about himself, who asks another person to help him. The fact that the doctor-patient relation is a relation of persons provides certain principles in itself. Just as a teacher who teaches his subject and not his pupils is a bad teacher, so a doctor who sets out to heal diseases instead of healing people will not be a good doctor. The patient as a person requiring help is the focus of all problems in medicine. If medicine treats disease, then a classification of diseases into bodily and mental will arise in which the unity of the person is lost sight of. Physicians and psychotherapists will have different objects to treat, and the necessity of co-operation in treating a patient who is always suffering in mind, whether or not he is suffering organically, will be lost sight of. Every case which a doctor deals with arises because of the patient's anxiety about himself. His anxiety, which brings him to the doctor, is his sense that something is the matter with him. The task of the physician is to discover what is the matter. If some malfunctioning of the organism can be discovered, then it can be correlated with the anxiety of the patient about himself. If this is correct then the restoration of proper bodily functioning will remove this anxiety and bring the relation of doctor and patient to the end. But if the doctor can assure himself that there is no organic failure sufficient to account for the anxiety of the patient, what is to to be done? The physician may feel inclined to say that there is nothing the matter with him. But there must be something the matter with a man who comes to a doctor when there is nothing the matter with him.

The anxiety must have a cause. As it is an anxiety about himself the cause must lie in himself. If it has no observable bodily correlate, the anxiety itself is a disease, and expresses the patient's sense that something is the matter with his functioning as a human being.—Professor John Macmurray (*A Philosopher's View of Modern Psychology*. Lancet, 1938). *The Quiet Art: A Doctor's Anthology*. Compiled by Dr. Robert Coope, Edinburgh & London, E. & S. Livingstone Lts., 1952, p. 230.

IV. Diagnosis And Therapy

D. A Suggested Plan Of Medical Action

Marshall Brucer, M.D.

Suggested Order Of Procedure For Any Person Involved In A Radiation Accident

	DEFINITIONS	*First Duty*
Worker	any person who has an accident	confine the hazard
Helper	any intelligent nearby person	protect the worker
Supervisor	any person with the authority to act	protect other persons
Contamination Accidents	radioactive isotopes; if doubtful, assume contamination	confine the hazard
Noncontaminating Radiation Accidents	X-ray tubes—distant explosions; neutrons or heavy particles not involved	stop source of radiation if possible.

PROTECTION CONSISTS OF THREE THINGS

TIME—work fast

DISTANCE—get away

SHIELDING—get behind something

A RULE OF THUMB

Physician should WORRY at	100 roentgens 1000 microcuries
All others should ACT at	10 roentgens 100 microcuries

Procedures In Contamination Accidents

Worker
1. Do NOT try to clean up.
2. Close windows, stop fans, block door.
3. Call for help,
4. Remove clothing,
5. Shower with soap and water.

Helper
1. Report accident,
2. Help clean up worker
3. Monitor worker.
4. Confine contamination.
5. Monitor yourself.

Supervisor
1. Stop all radiation work,
2. Seal area,
3. Monitor all personnel.
4. Consult wih experts,
5. Clean up.

Procedures In External Radiation Accidents

Worker
1. Run,
2. Call for help,
3. Turn off machinery,
4. Block area,
5. Rest—let George take over.

Helper
1. Report accident,
2. Make worker comfortable,
3. Block access to area,
4. Monitor worker,
5. Monitor yourself.

Supervisor
1. Turn off source,
2. Block access to area,
3. Hospitalize at 100 r,
4. Check all possible exposures,

5 Consult with experts.

Suggested Order Of Procedure For Physicians Involved In A Radiation Accident

FIRST PHYSICIAN ON SCENE OR DISPENSARY PHYSICIANS

1. Remove patient from area.
2. Give immediate first aid.
3. Call for Health Physics help.

4. Isolate patient to prevent infection (and contamination of others).
5. See that danger area is closed off.

(These first five procedures are not the business of a physician, but he must make sure they are done.)

6. Sit down—throw out visitors—think—and answer two questions:
   a. Is the patient contaminated? With what?
      Were neutrons or heavy particles involved?
   b. What is the approximate level of radiation exposure?

CONTAMINATION	**NOT CONTAMINATED**
(If in doubt, assume contamination)	
7. Clean up gross contamination—remove clothing, preliminary wash.	7.
8. Measure contamination approximately — (whole-body counter is ideal, any instrument is adequate).	8.
9. Put patient to bed.	9. Put patient to bed.
10. Save all samples: clothes, blood, urine, feces, vomitus, hair, nails, sheets (use currrent newspapers for wrapping; they can be presumed to have little radioactivity.	10. Save biological samples: blood, urine, feces, vomitus, hair, nails.
11. Do routine blood count, freeze and store a 10 cc sample of blood.	11. Do routine blood count, freeze and store a 10 cc sample of blood.
12. Give sedation, if indicated.	12. Give sedation, if indicated.
13. Send patient to hospital if you suspect more than 100 r exposure.	13. Send patient to hospital if you suspect more than 100 r exposure.
14. Brief the administrator and the public relations office.	14. Brief the administrator and the public relations office.

Hospital Physicians

15. Save all samples, wrap anything that may have come in contact with the patient in current newspapers; wear scrub suit and rubber gloves.	15. Save biological samples.
16. Do brief history and physical.	16. Do brief history and physical.
17. Do emergency surgery if indicated.	17. Do emergency surgery if indicated.
18. Do definitive surgical decontamination. Health Physics help is needed and you may have to do 17 and 18 simultaneously.	18.

19. Do definitive survey of patient; whole-body counter is ideal, but use whatever instruments are available.
20. Forestall iatrogenic exsanguination. Most health physics can be done with urine samples.
21. Start frequent lymphocyte counts.
22. Give sedation if indicated.
23. Give antiemetics if indicated.
24. Do definitive history and physical.
25. Start definitive laboratory work.
26. Review history and physical examination of patient and the accident situation with physicians and health physicists.
27. Brief administrators and public relations office.
28. Record events, exact times, and estimated dosages.
29. Call for consultation with experts on radiation damage.
30. Revert to routine hospital procedures.

V. The Problem Of Protection

A. From War Time Explosions. How Many People Are Involved?

Joseph D. Goldstein, Col. MC*

■ How many people will be involved in a radiation accident: this is a simple question without a simple answer.

Any answer demands a clear definition:

(1) The circumstances of the event: We will assume a sudden, albeit intentional rather than accidental, release of uncontrolled nuclear energy—a nuclear weapon detonation.

(2) The purpose for the prediction: The appraisal will direct itself to the kinds and numbers of injured which will not only require but will reach medical care, and hereafter will be referred to as the medical load.

The well-known "agent-host" relationship lends itself well to a basic analysis. The agent in this case is a sudden release of nuclear energy. It dissipates itself in three ways: as blast, heat, or ionizing radiation. The relative partitioning of the total energy may vary significantly from accident to accident. Some of the influencing factors are the chemical composition, size, configuration and environment of the exploding mass. Clinically the differences may manifest themselves over a range from severe, combined mechanical, burn and radiation trauma through a wide spectrum of injuries down to mild or subclinical ionizing radiation exposure. Because of the wide spectrum of hazards, a detonation has all the ingredients built into one situation. The physician may gain an over-all feel of the medical load by generalizing the types of casualties he might expect from different size weapons. The physician must remain acutely aware that any such generalization is susceptible to exceptions.

The Kind Of Injury

Accepting this stipulation, the physician may expect predominantly ionizing radiation injuries with some concomitant mechanical trauma to make up the medical load from small nuclear weapons such as the Davy Crockett. "Nominal" sized weapons (as used at the end of World War II) should contribute a combination of all three types of injuries: mechanical, thermal and ionizing radiation. Megaton (the so-called H-bomb) weapons probably would result in shifting the complexion of the medical load toward an increase in thermal injuries with a lesser increase in mechanical injuries.

Geographical Location Of Detonation

If a weapon is detonated as a surface burst, ionizing radiation injury would occur in many of the burned and mechanically injured survivors located concentrically around ground zero. In addition, injuries directly attributable to downwind fallout would be due to ionizing radiation *per se* without mechanical or burn trauma. Downwind (local, close-in) fallout should be differentiated from world-wide (distant) fallout in that downwind fallout is deposited in significant amounts in a matter of hours and for distances not exceeding a few hundred miles from the time and place of detonation. World-wide fallout may be deposited for years and at points measured in thousands of miles. Another difference is that downwind fallout currently merits consideration primarily as an external hazard, whereas world-wide fallout can primarily be considered an internal hazard.

Under the current, openly expressed concepts for nuclear weapon employment, the medical load due to ionizing radiation by itself or in combination with other types of trauma would be a significant, formidable medical challenge. This point has special impact when one considers the summed effect of combined injuries. There are disturbing indications in the Japanese data. They show a death rate in burned patients which is excessive from that expected from burns alone. Some experimental data on laboratory animals confirms this impression. Further, one must realize that, despite prodigious research effort, therapeutic countermeasures against acute radiation injury are aimed at the complications of radiation injury and are essentially supportive rather than specific.

Let us now turn our attention to the host, man. Obviously, the mere liberation of injurious forces from a nuclear source does not produce medical problems until such forces are exercised upon man. It follows that the end result will depend on the type and degree of exposure that man will present to these forces. This relates man inextricably to his environment. Normally this environment changes in some manner in time either from choice, necessity, or natural processes. Such changes could work for or against protecting man. For example, a built-up urban area might contribute many injury-producing missiles not found in an open field but at the same time offer shielding by intervening building from flash thermal radiations which would not be afforded in an open field environment. In addition, the very structures protecting against flash burns may provide the fuel and necessary conditions for secondary fires with incident flame burn and smoke inhalation casualties. These environmental factors will also affect the amount of ionizing radiation delivered to the individual because of variable shielding factors. Briefly, environmental differences, whether natural, structural or personal, could modify the medical results by either diminishing or increasing vulnerability to blast, thermal or ionizing effects.

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Time

An important factor is time—time during which one can take evasive action by changing his environmental setting. This is especially, but not necessarily exclusively true when dealing with downwind fallout which can cause radiation sickness. One is exposed to downwind fallout by having it come to him or by his coming to it. In both cases time works in favor of the potential victim. Hence, the delay engendered in travel of fallout permits a decrease in its radioactivity by an inherent decay. The longer the time, the more the decay. This is particularly effective during the early hours post-detonation when the decay rate is most rapid. As a rule of thumb, the radioactivity of mixed fission products in fallout decreases to one-tenth its value for every factor of seven in time. This means that a reading of 100 rad/hr at one hour after a nuclear explosion will be about 10 rad/hr at seven hours and about one rad/hr at the end of two days. This characteristic decay scheme reduces the one-hour reading to less than 50 per cent in two hours. When translated into transient times (not considering any further dilution) with an effective wind of about 15 miles per hour, more than 50 per cent of the first hour intensity will have been dissipated before it can affect an individual 15 miles downwind from ground zero. This fact must always be considered when predicting the amount of radiation to which people might be exposed at any given point. The importance of the time factor becomes greater with large weapons capable of having fallout patterns extending a few hundred miles.

Distance And Shielding

A second and third way in which time works in favor of the individual pertains to evasion. A nuclear detonation in the atmosphere may be identified immediately because there is an intense flash of light which travels at a speed of 186,000 miles per second and can be seen over long distances. In contrast, fallout usually travels with the speed of the prevailing wind, which averages about 15-20 miles per hour. The time interval between the flash and the arrival (and subsequent build-up) of the fallout levels permits evasive action which could approach complete protection, depending on the state of preparedness. This time interval also may allow medically significant action from thermal radiation and blast effects in the concentric area around ground zero at distances of medical interest.

In short, the amount of injury sustained by an individual from the weapon effects is a function of the distance (or shielding), therefore time, between the point where the injurious agents are released and the point of physical occupancy of the host.

The Number Of People Involved

The number of casualties may be estimated before a nuclear event by a straightforward method of superimposing the ranges of the various weapon effects as an idealized pattern over a given target. An example of such an idealized pattern is the well-known concentric annuli around ground zero and the cigar-shaped downwind fallout contour. Experience has shown that, whereas the pattern around ground zero shows a reasonable agreement between theory and practice, any similarity between the post-detonation fallout pattern and the predicted one is exceptional. The discrepancy does not stem from lack of knowledge alone. There is discrepancy simply because one cannot, with certainty, tell what the various winds up to about 40,000 feet may do. Prudence dictates that for purposes of medical planning the least favorable situation should be selected, At the present state of the art, such procedures, however detailed and precise, should never be considered as ultimate knowledge. Without further belaboring the point as to its merits or deficiency, for the sake of discussion, we will consider the procedure as acceptable.

It is obvious that all one gains by such a map manipulation is simply an "area coverage" of so many square miles. This still does not tell us how many people will be affected. It is fundamental that to injure people, they must be present to be injured. Admittedly, if one chooses a densely and homogeneously populated area, large numbers of casualties will be predicted. If everyone in the open takes no evasive action and is denied even the benefits of simple terrain or structure masking them, everyone will receive the full impact of the weapon effects. A detailed appraisal of any selected target usually points up the necessity for adjusting for different population densities and environmental variables within targets.

Although pertinent variables such as weather, season, warning time and state of preparedness cannot be neglected, the mere recognition and introduction of such multiple, although essential, variables demonstrate the uncertainties inherent in predicting how many people will become casualties.

This is especially true where predictions are based on a relatively small number of targets and variety of nuclear events. In essence, because of the immediate saturation effect and characteristics of nuclear weapons, large percentages of the population put at risk around ground zero can be expected to become casualties if a weapon is accurately delivered on an appropriate target. In counterdistinction, much smaller percentages of the population in the downwind fallout pattern may be involved because people can take initial advantage of available shielding as soon as possible and continue to improve such protection during occupancy. The reduction of the numbers of potential casualties by such measures becomes self-evident when the large areas of possible coverage are noted, even though the average population densities in the downwind area probably will be less than around ground zero.

Rescue Factors

Other factors may strongly influence the magnitude of the medical problem. The assumed exposure of the individual and the assumption of the merging injured does not necessarily reflect the numbers which will make up the medical load presenting themselves for medical care. This will depend on rescue. Even under optimum conditions, the policing of a large area for casualties takes time. This time lag can be expected to be lengthened appreciably when rescue operations are hampered by residual radiation, rubble, or sheer numbers. In any case, one comes to a painful realization that nature may effect her own attrition because of an inordinately long time lag between injury and care. For any estimate to be medically meaningful and useful, clinical criteria for casualty production, hospital stay-time, and ultimate fate must be defined and stated thoroughly. All in all, the mere relationship of a weapon to a target can become just an exercise in numbers unless a sizeable effort is made to clinically evaluate the types and numbers of casualties which may emerge so that a studied plan can be made as to what to do, where, when, by whom, and for how long.

A prediction of the medical load is unquestionably a useful tool when due consideration is given to the limitations of the method employed for making the prediction. This quantitative appraisal, when combined with the types of casualties generated, helps define a problem. The statement of the problem gains meaning and value to medical planners when it is related in time and space to an estimate of predicted medical resources.

Foreseeably, with the medical load there will be a concomitant attrition of medical resources due to medical personnel casualties and destroyed facilities. It follows that in the early post-detonation period and in the vicinity of ground zero, a serious disparity between needs and means may develop; whereas, during the later recovery period and in the relatively uninvolved areas, this disparity may be minimal. Obviously the "numbers" in one case have a very different implication from the "numbers" in another case. There is a large dependence on sorting and treatment policies. Finally, "numbers" may also help to create a stimulating awareness of the possible magnitude of the problem. Of greater importance will be the recognition of how these "numbers" might be significantly reduced by a well-informed and prepared community. The crux of the matter is that "numbers" should not only indicate a possible and painful price in morbidity and mortality but should motivate and compel everyone to prepare in order to preclude paying any price greater than that which is absolutely inescapable.

Rejoice also in tribulation; knowing that tribulation worketh patience; and patience experience; and experience, hope.—Romany.

V. The Problem Of Protection

B. From Peacetime Reactors. There Are People To Protect†

Hugh F. Henry, Ph.D.*

■ The principle hazard of a criticality accident is the possibility that nearby individuals may be suddenly exposed to neutron and gamma radiation. Neutrons are emitted during the reaction itself but not when the reaction has ceased. Gamma radiation is emitted both at the time of the reaction and subsequently from radioisotopes. Normally, criticality accidents will start with a high-level burst followed by more or less extended lower-level reactions, perhaps punctuated by intermediate bursts. It appears improbable that peacetime accidents will have explosive effect or even that the immediate results will be as spectacular or devastating as may occur from a pressure vessel or chemical explosion. Adequate personnel protection against radiation, even from an accidental criticality excursion, is routinely provided as a part of the usual Health Physics program where critical conditions are normally attained or expected, as with reactors or experimental critical facilities.

The problem of personnel protection at a criticality excursion is significantly complicated by the fact that:

1. The initiation of an accident requires only the accumulation of excessive fissionable material and a favorable configuration and may not involve a readily recognizable physical change such as that of temperature or color.

2. There is essentially no known way to measure an approach to criticality; the system is apparently safe until proper conditions are reached and it then becomes critical.

3. There is not necessarily an obvious and readily recognizable indication that an accident has occurred.

Time

Basic to protection is prompt notification to all personnel in the immediate vicinity that an excursion has started or has occurred. This can be done with audible or visual alarm systems, but they must be distinctive, of rapid response, and immediately evident to people over a wide area for the smallest burst that can be foreseen. The alarm system should be both "fail-safe" (should not give false signals) and should not be used for any other purpose.

Distance

Essentially the only action that an individual can take to limit his own exposure following a criticality accident is to get away from the site as quickly as possible. If he knows the general location of accident, as in a laboratory activity, he should run away from it. If its site is equally probable for any of a large number of locations, as in chemical recovery or fuel-rod manufacturing facilities, he should run out of the operating area as promptly as possible and then go to a point which he knows can't be the accident site. This would usually mean that he would leave a building that has well identified exits for this purpose.

It is, of course, possible that an individual may unknowingly approach and pass near the site of an accident as he runs for the nearest exit. However, if he is running, he will probably receive only a comparatively low dose, which, although high by normal "permissible limits" figures, may not be hazardous. On the other hand, if he is standing near the reaction at the time it occurs and for some reason does not get out quickly, he could receive a dangerous exposure.

Shielding

A criticality accident in operating areas only generally known will probably affect proper design even in locations so remote that individuals would receive negligible exposure. Similarly, an individual, although near the burst, may himself be fortuitously shielded, perhaps by items of equipment, so that his actual exposure would be very small.

Personal Dosimeter

To provide effective medical treatment, it is necessary to separate high-exposure from low-exposure patients. This separation may be readily made if each individual in the operating facility routinely carries a few grams of one of several neutron-sensitive metals. These neutron-sensitive "foils" are sufficiently activated by even low neutron exposures so

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[†] *A more detailed treatment is given in* Progress in Nuclear Energy, Series IV. *"Technology, Engineering, and Safety," Vol. 3, edited by C. N. Nicholls, Chapter 3-2, pp. 206-227, "Planning for control of criticality emergencies," by H. Henry, Pergamon Press, 1960.*

that the resultant beta-gamma emission can be readily detected with a simple survey meter. Of these foils, indium is perhaps the best all-around material, with gold, manganese and copper among others, also being useful. In practice, the neutron-sensitive foils would be collected promptly from all potentially exposed individuals and checked with a beta-gamma survey meter. Since the foils are sensitive only to neutrons, they will not be affected by routine gamma exposures nor will they be activated by the fission-product radiation following cessation of the excursion itself. For the gamma radiation, film badges may be combined with the metallic foils.

There is, unfortunately, no simple device which an individual may wear to provide a method for readily determining his radiation exposure by a factor closer than about 3 to 6. Probably the most important of the conditions which complicate such dose determinations is the relative orientation of the individual, his personal monitor, and the site of the accident. However, difficulties are also presented by the characteristics of the excursion itself. Probably the best method of dose determination involves a rather complicated system of blood sodium activation evaluations coupled with information obtained from a system of area dosimeters placed throughout the facilities. Whole-body counts have also been suggested. Such complex techniques may give a closer indication of the dose received, but they are time-consuming and require considerable evaluation skill.

Contamination of the air and surfaces by fission products and other radioisotopes during and following an accident may present problems in addition to those from direct radiation. Although it is extremely unlikely that any significant internal exposure can result from such "fallout," there is a possibility, particularly in chemical operations, that spattering or even missile injection can be carried some distance from the accident. In general, significant contamination of an individual's clothing and skin may be readily detected by a survey meter. Since such contamination will increase the exposure of an individual, it must be eliminated by removal of clothing and by bathing.

Administrative Action

Administrative actions are very important to personnel protection in locations where criticality accidents can occur. Among the precautions which should be taken are those to insure that:

1. None of the individuals who were potentially exposed at the first burst can re-enter the area for any reason until their exposure is determined and such re-entry is known to be safe.
2. Extreme caution is taken in approaching the identified site of the excursion until it is known that it has stopped.
3. Needless exposure to "sightseers" will be avoided; this particularly includes management and supervisory personnel.
4. Efforts to stop the reaction and thus make the system subcritical are taken with people as far away from the site of the excursion as possible; it is not impossible that such activities may "retrigger" the excursion.

Protection Preparations

It is prudent to prepare for a criticality accident if there is even the slightest possibility of its occurring. The following actions are necessary:

1. Careful preplanning to meet emergencies.
2. Provision of alarm devices.
3. Training to urge all employees upon hearing a radiation alarm to run, not walk, to the nearest exit and then get away from the possible site of the accident.
4. Require all individuals that might possibly be exposed to have on their persons a neutron-sensitive metal. There must also be provisions to read the neutron-sensitive devices following an accident. The whole purpose of neutron-sensitive metals or gamma-sensitive film badges is to allow quick separation of the relatively unexposed from the more highly exposed.
5. Recognition that extreme care is needed in approaching and otherwise disturbing the reacting material until it is positively known that it can no longer attain criticality.
6. Provisions for decontaminating people.

V. The Problem Of Protection

C. In Routine Clinical Practice. The Radiologist And Radiation Hazards

Herbert D. Kerman, M.D.*

■ On June 8, 1956, the National Academy of Sciences reported to the public on the biologic effects of radiation.[1] Since that time the public and the medical profession have been bombarded with numerous publications on the subject. Newspaper, magazine and journal articles have been abundant and have abounded in erudite expressions of opinion. The radio and television commentators have mixed fact with fancy; and generalities, misinformation, and just plain bunk and nonsense are the rule. It is no wonder that the average man is bewildered and a little bit frightened about the hazards of radiation. The topic of radiation has become one of the most cogent and controversial subjects involving the medical profession and the public in many years.

Physician's efforts in radiation protection began shortly after the discovery of X-ray. By 1920, the American Roentgen Ray Society had formed a committee to recommend protective measures. The committee expanded under the auspices of the National Bureau of Standards until in 1946 it became the National Committee on Radiation Protection. For over 40 years the philosophy of the National Committee and of all radiologists has been to expose patients and employees to the least possible radiation consistent with medical necessities. Radiologists have long been aware of their obligations in regard to radiation hazards. Indeed, the entire atomic energy program owes its excellent radiation protection record, in large part, to the contributions and advice of the radiologists associated with it.

To understand radiation protection, one must first be aware of the nature of the radiation hazard. The radiation hazard is a *real* hazard, and deleterious effects of radiation to humans may be manifested in either somatic or genetic changes.

Somatic Effects

The somatic effects of radiation in humans have been well documented. The serious late sequelae of *intensive radiation* and the development of skin changes, atrophy, pigmentation, telangiectasia and the serious effects of tissue necrosis, sterility, radiation cataracts, congenital abnormalities, retardation, of abnormal growth, aplastic anemia and radiation neoplasia are well documented phenomena. To know that the hazard is real, one needs only to recall the stone monument at the Roentgen Institute of Hamburg inscribed with the names of over 300 martyrs who were unwittingly overexposed to radiation prior to the recognition of radiation hazards.

However, the *alleged* somatic effects of congenital abnormalities, sterility, carcinogenesis, leukemogenesis and life-shortening due to *partial-body low dose* or *single low dose* are less well documented; in some respects they are open to serious question. So often both experimental and clinical investigations in these categories have been presented with such great enthusiasm and "mathmanship," that credence in the observations is wholly unwarranted. Nonetheless, these reports cannot be wholly denied and must be considered. The unproved as well as the proved effects impose a definite responsibility to users of ionizing radiation.

Genetic Effects

Radiation, undoubtedly, causes mutations. Muller's[2] Nobel Prize winning work with fruit flies has been strengthened by Russell's[3] work with mice. In all the animals studied there is a general agreement that the rate of mutation is increased by irradiation. There may or may not be a dosage threshold below which genetic effects do not occur. But there is also general agreement that gonadal exposure *may* be genetically harmful. Data from studies of mice have allowed various estimates of the amount of radiation exposure necessary to double the mutation rate in man (probably between 30 and 80 r). The mutations may not be observable as gross physical abnormalities, but since all of the mutations are deleterious, (?) however slight, they must be seriously regarded. These mutants are not easily lost but may perpetuate silently for many generations, so despite the uncertainties, they must be vitally considered.

However concerned about radiation-induced mutations, the physician must also keep in mind many other mutation-inducing factors. Oxygen tension, most chemicals and even such a simple thing as temperature elevation can produce mutations in experimental animals and, presumably, in man. If we are to view with alarm the consequences of doubling the mutation rate, we should first be amused by the report of Ehrenberg[4] and co-workers that the wearing of trousers increases the male gonad temperature by 3° which may cause almost half of the present load of spontaneous mutations. This leads to a sober recommendation for the wearing of kilts as most important in decreasing spontaneous mutations!

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* *Daytona Beach, Florida.*

Thus, the radiologist is wholly aware of the nature of radiation hazard. Despite uncertainties in degree of hazard and dosage, the radiologist always has been and is now, even more vitally concerned with the problems of radiation protection. There could be no better credo in radiation usage than to "keep the dose as low as possible."

What Is Being Done To Achieve The Lowest Possible Exposure?

Protection must be afforded to three general categories of personnel:

1. The patient must be protected.
2. The physician and technicians employing radiation must be protected.
3. The "innocent bystander" must be protected.

Patient Protection

The qualified radiologist is trained to use factors that combine use to permit an examination that will reveal the most diagnostic information with the least possible exposure. Patient protection involves stringent adherence and meticulous attention to relatively simple and readily available procedures and techniques.

By far, the most important feature is the proper indication for a radiation exposure. Unnecessary radiographic examination should not be undertaken any more than unnecessary administration of drugs. The X-ray is not a short-cut to a proper history, physical examination, laboratory examination, or the intelligent deduction required of good medical practice. Since most radiological practice is referred, the radiologist must educate his nonradiologic colleagues as to the proper examination for the individual problems. He must not allow himself to be pressured into unnecessary examinations and the final decision, as to whether an examination is indicated, rests with him. Radiographic examination of the pregnant abdomen and the gonadal areas of those persons in child-bearing age should be undertaken only for compelling medical reasons. Routine X-ray examination should be avoided. Periodic X-ray surveys should be restricted to "high yield" groups.

Photoroentgen case finding surveys must be scrutinized carefully to be properly justified. It should be recalled that the exposure of a conventional optic type of photoroentgen unit is 8 to 10 times as much as conventional 14" x 17" film and the mirror optic systems yield 3 to 5 times as much exposure as a full-sized film.

Competent performance of technique entails accurate limiting and filtration of the primary X-ray beam. Full use should be made of the proper distance. The most sensitive combination of films, screens, developing chemicals and temperature, and the use of high kilovoltage that will permit satisfactory contrast. The reduction of the number of films and fluoroscopy time of each examination is extremely important.

Fluoroscopic examination could contribute the most radiation exposure to both patient and physician of any technique in diagnostic X-ray examinations. Yet, the fluoroscopic examination is probably the least valuable procedure when done by an untrained physician, and particularly when it is an isolated procedure. Recently, Sherman,[5] in pointing up the limitations of isolated fluoroscopy, has suggested as an axiom, "Film first—fluoroscope later—if indicated." When fluoroscopy is employed, the measures of proper dark adaptation, maximum tube-screen distance, small field size, low milliamperage and time limit controls are essential. Developments in image amplification hold great promise as a useful technique to reduce exposure.

Radiation therapy occupies a small but important part in the radiation exposure of some patients. The judicious use of radiation therapy for benign lesions is sometimes very helpful. However, if there is a choice of other therapeutic measures, and if all things are equal, then the other method of treatment should be preferred. In many cases, radiation therapy is of limited or doubtful benefit. The choice of treatment is the responsibility of the physician, not the patient or referring physician. Radiotherapy for malignant disease usually has benefits far outweighing the calculated risk of possible adverse radiation effects.

The Physician And His Technicians Must Be Protected

The physician's protection of himself and his technicians is, primarily, a matter of discipline. The rules are simple—time, distance and shielding. Fluoroscopy should be kept to a minimum and those in the fluoroscopic room should wear aprons. There are mechanical methods available for mobilizing patients. It is not permissible for a technician to hold or support a patient during exposure. Exposure switches must be so arranged as to not permit the technician to be exposed. Personnel monitoring must be understood and has become a routine procedure. When simple regulations are understood and enforced, adequate compliance with accepted permissible limits for radiologic workers is not a problem. In 1956, when even better discipline and even more meticulous attention to details were enforced, a good radiation exposure record was made even better.

Most of my own exposure was obtained, not in fluoroscopy, but in using radium. This technique is a particularly difficult exposure problem. Extraordinary care in the use of barriers, remote handling equipment, rapidity, dexterity and prior planning is essential to reduce exposure.

Protection Of The "Innocent Bystander"

The innocent bystander is the secretary in the next office, the clerk in the office below, the receptionist in the corridor. The principle ingredients of protection are the same as for the radiologist—time, distance and shielding. In planning X-ray facilities, all of these problems bear careful scrutiny. Compliance with the recommendations of the National Bureau of Standards Handbooks of Radiation Protection are essential. The technical information for proper shielding, design and layout of X-ray equipment is readily available and there is no excuse for noncompliance. Protection surveys must be made. Personnel monitoring systems should be employed. Calibration and measurement of individual X-ray units is essential, so that accurate knowledge of radiation output of each unit is known with different technical factors. Ordinarily there is a wide variation of dose so that the published reports and records of one institution cannot, in general, be applied to another. The dose can, and should, be measured for each unit to provide data for a particular examination and to focus attention on genetically significant techniques. The qualified radiologist does qualify as an expert in this respect. Radiation physicists may be called upon to assist or advise in unusual situations.

Medical Use Presupposes Responsibilities

These, then, are the direct obligations and responsibilities of the radiologist to his patient and personnel in the use of ionizing radiation in medicine. These same obligations and responsibilities are also imposed on any and all persons other than trained radiologists who may use radiant energy in the healing arts. There are only 5,000 certified radiologists, but there are possibly 35,000 other doctors, excluding osteopaths and chiropractors, and 65,000 dentists who use X-ray equipment. In addition to his own obligations, the trained radiologist has an indirect responsibility to educate untrained users of radiant energy.

The American College of Radiology has made a major contribution in this area by recently distributing a practical manual on the medical and dental uses of X-ray with control of radiation hazard. Further educational activities are progressing, but the basic responsibility will always rest upon those employing radiant energy and the highest professional standard is the only valid method of insuring good practice. Legislative bodies are now cognizant of radiation hazard, and radiologists are striving for adequate but nonrestrictive codes and regulations. The responsibility of the radiologist in this respect is indeed large, and it is urged that all of organized medicine insist upon competent and adequate radiologic advice in developing such legislation.

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VI. What Does The Rest Of The World Think?

Foreign Opinions On Nuclear Accidents

Marshall Brucer, M.D.

■ Nuclear accidents will not be confined to the United States. After all, the first nuclear reactor would have been Canadian or French if enough material had been available. The roster of scientists who have contributed to the release of nuclear energy reads like an international telephone book. Probably the most hilarious (if it weren't so sad) scientific joke of the century was when the American Congress in 1946 vowed to keep "the secret." Only a small portion of the ever increasing secrecy has military justification; most is bureaucratic empire building. In surveying a large number of foreign scientists for their opinions on nuclear accidents, I was struck by three kinds of answers:

(1) the number of people who could not answer because anything nuclear is a political hot potato;

(2) the vast number who thought the problem unbelievably simple—"just send the patient to the nearest doctor";

(3) the awareness that the *medical problem* is not confined to physicians.

In gathering these comments by non-U.S. experts, I specifically requested that the official government opinion be subordinated to personal opinion, because official government documents are invariably useless committee reports.

Switzerland

REMARKS ABOUT NUCLEAR ACCIDENTS IN SWITZERLAND

Professor J. H. Muller, M.D.*:

Radiation protection is ruled in Switzerland by *federal law*, based on internationally accepted standards. The careful regulation of the uses of ionizing radiation and of radionuclides covers all medical and industrial activities and will soon be ready for effective use.

There are special problems in the operation of *high-energy particle accelerating machines*. Potential accidents would be limited to a small number of persons and to partial-body irradiations. Therapeutic measures would then be of a rather specialized type. The health physics control in these laboratories is reliable.

Several *education and training type* reactors are now operated in Switzerland (Universities of Geneva and Basel) or of the *research and testing type* (Diorit and Saphir in Wuerenlingen, this main nuclear center being now an out-department of the Swiss Federal Institute of Technology of Zurich). There has been no significant accident yet in connection with these reactors. There is, however, a definite trend towards organizing emergency medical service in co-operation with the local University Medical Center. In the case of the Wuerenlingen Center, about 30 miles from Zurich, the nearest District Hospital was contracted for first emergency service. Facilities for whole-body counting will be soon available in Geneva and in Zurich.

No reprocessing plants will be run in Switzerland, at least for the next decade. Similarly, highly active wastes will not be kept in the country, but will be sent for storage to the "Eurochem" in Mol, Belgium (possibly also to England and France). These safety factors are, for the time being, of limited practical importance since no *power reactors* are yet available in Switzerland. However, excavation has begun at Lucens, where the first Swiss power reactor is scheduled for 1964 completion. It is highly probable that in the future larger units will be constructed. The hydroelectric power potential of this country is nearly exploited to its maximum.

The wartime situation is different. The probability of direct hits of atomic weapons may reasonably be considered small. Switzerland has a status of eternal neutrality and nuclear aggression has a strategic uselessness. It is quite likely that this country might be heavily affected by radioactive fallout if an atomic war should ever be fought in its neighborhood. The people and the government are conscious of such potential danger. The building of tight shelters has been made compulsory in practically all new construction.

It is striking that among the medical profession true radiation consciousness is in a rather latent state. There is some uneasy feeling about it. Practically all physicians should be in a position to use a simple radiation detector. It is quite clear that in any presumed or real nuclear emergency the medical profession will naturally become besieged by the anxiety of people fearing for their health and seeking immediate help. It should be expected that even imaginary dangers could raise panic. The panic might be stopped if each physician has a monitoring instrument of his own.

What the physicians of this country would do about patients should such accidents occur is to seek close co-operation with larger hospital units that are already (to a certain extent) equipped with supplies of the materials necessary for adequate care, according to published world-wide experience. Special literature on nuclear accidents is available throughout the country.

The first condition for this task would be, obviously, the survival of the doctors and of their aides . . .

Sweden

Switzerland is unusually endowed with large machines, excellent facilities and exceptional physicians; so is Sweden. Dr. Sven Benner, a Ph.D., also an M.D (but honorary) passes the diagnostic and therapeutic questions off to the hundreds of more qualified physicians in Sweden but brings up another problem that hasn't yet been considered. (Incidentally, the *sealed sources* he speaks of have already caused (?) three deaths in Mexico.)

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* Department of Radiology and Pathology, Frauenklinik, University of Zurich, Switzerland.

POSSIBLE FUTURE HAZARDS FROM SEALED RADIATION SOURCES

Sven Benner, Ph.D.*:

> Industrial, medical and other radiation sources can often be used for their original purpose only for a half-life or two. They may still be sufficiently active to be a potential hazard for several centuries. Sources may also be removed from practical use long before their activity has decreased appreciably because the rapid technical process has rendered their design or use obsolete. While not at all comparable in magnitude with the problems of large-scale atomic energy wastes, sources may in the future constitute hazards that cannot be neglected and may occasion rather strict legal and organizational measures.
>
> What does management do with such sources? It takes money, time and space to keep them securely stored, protected from fire, pilfering and other hazards. It is also a problem to keep active, up-to-date records which themselves must be well protected and interpretable after hundreds of years. Management may be reluctant to spend much on sources which no longer give profit.
>
> The answer may be that the A.E.C. (Sweden), or its equivalent in other countries, takes care of the problem by periodic inspection at the users' premises and by taking back those sources which are no longer used and which are not adequately taken care of by the possessors. Maybe, but consider the extent of the files necessary to keep accurate, up-to-date records of thousands of sources all over the country in the most varied types of plants—industrial, agricultural, scientific, medical, etc.—and of all the inspection reports. Will there not occur errors now and then, so that some sources are lost track of? And what to do if the records are partially or wholly destroyed? Or if the A.E.C. and the political system we now have should cease to exist?
>
> Returning to conditions more similar to the present, there must necessarily be some time between successive inspections. Virtually anything may happen in the meantime. The sources may be destroyed by accident, or irretrievably lost, or a firm goes bankrupt and its possessions are scattered in various directions. Is it certain that the buyers will notice some insignificant-looking metal pieces? What can the A.E.C. do in such cases? Where nothing remains to be taken, the emperor has lost his right.

Dr. Benner's point is that we don't know what is going to happen in the future. Dr. Muller's point is that at least in Switzerland they are going to be prepared before the accident occurs. Dr. Benner's fears have already been amply demonstrated. Opening a sealed source in Houston resulted in a severe psychological disease. It also put a plant out of business.

In 1958, an *unleakable* sealed teletherapy source in Oak Ridge leaked Co^{60}. A rapid country-wide survey revealed that 10 per cent of *unleakable* sources were leaking. In Mexico City an industrial radioisotope source was used as a toy and caused (?) three deaths. These things can't happen, but as Dr. Benner points out, maybe they can.

Venezuela

Dr. Marcel Roche, (M.D.), is director of the Instituto Venezolano de Investigaciones Cientificas (I.V.I.C.). He writes concerning what is available to cause accidents in a small country and what plans they have for taking care of the medical problem

> As you probably know, we have here at the Institute a 3-Mw swimming-pool reactor, but it is actually shut down and will continue to be so until a number of young people return who are now doing postgraduate studies abroad in the field of Physics, and especially in Nuclear Physics. In the meantime, the potential for nuclear accidents in our country depends entirely on whatever the two large nuclear powers wish to do with their weapons.
>
> We have here at the Institute two scientists who are interested in the treatment of irradiated patients, both of them hematologists. Another is interested in the matter and has recently attended a special course at the Weizman Institute in Israel. It is my intention, before the nuclear reactor is put to work again, to have these men draw up a definite plan including the logistics and the therapeutics for dealing with medical nuclear accidents.

Probably the essential thing that Dr Roche is concerned with at the very beginning of even a small program is preplanning for an accident one hopes will never occur.

Japan And England

Japan is probably the most highly industrialized country in the world (including the United States, England, Switzerland, etc.). It is already using its hydroelectric potential to a maximum. It has no significant fossil fuel deposits. England has small hydroelectric potential and it has depleted most of its significant fossil fuel deposits. The Japanese islands are about one and one-half times larger than the British Islands; the population is about double. Both peoples are highly literate. The Japanese probably have the highest literacy rate in the world.

The British published the first medical journal concerning radiation (even before the Germans), but the Japanese probably have the largest coverage at the present time. A significant portion (10-20 per cent) of the electricity produced in England is already by nuclear reactors. The Japanese intellectual development in the field of nuclear energy, at one time a few years behind England, is probably now ahead of, or at least equal to, that of England. The British have already tested a number of atomic weapons. They have the industrial and military capability already at hand. The Japanese have exploded no atomic weapon. They have the intellectual, industrial, and presumably the military capability of doing this on about a year's notice. The British have already had one large-scale incident (not accident) at Windscale, which was distinguished primarily for political mishandling and an ensuing public relations hysteria. There is probably a larger potential for radiation accidents in England than in other countries because of the large-scale use of radiation-producing devices. They had the first teletherapy machine in the 1920's (using radium) ; they had the first accelerator; they were probably the first to do routine diagnostic radiology; but the Japanese are not far behind.

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One of the first documents to seriously consider the medical problems that might be involved in nuclear accidents, especially large-scale accidents, was by T. E. Graham, Senior Medical Officer for the United Kingdom Atomic Energy Authority at Windscale, England. This was published as a confidential document in June of 1956 entitled, "Medical Memorandum on Criticality." The document summarizes the hazards, the production measures, the necessity for personnel monitoring, and describes the disease just about the way we would now describe it. Dr. Graham summarized the treatment of the Los Alamos patients with the words *treatment was symptomatic*. His summary of the four Argonne cases (June 1952) was *psychological reassurance*. For the two Russian cases, he quotes the Russians, *treatment consisted of bed rest, with penicillin, pyridoxin, glucose, and vitamins; transfusions and antihemorrhagic drugs were given, sodium nucleic acid, "tesan" and "tentoxyl."* There was a rather complete detailing of plans in future accidents.

The Japanese have had the only experience of a large-scale nuclear weapon detonation. This is being thoroughly investigated by the Atomic Bomb Casualty Commission (ABCC). By 1961 it had already published over 300 papers, usually both in Japanese and in English, and usually with both Japanese and American authors.

Dr. Hisao Yamashita writes concerning the Japan Institute of Radiological Science, which is only one of a number of organizations that has already preplanned their procedures for a radiation accident. The Japan Industrial Forum held its Fifth Japanese Conference on Radioisotopes in 1962. Since there is a relatively greater use of radiation and radioisotopes in Japan than in any other country, there is probably a greater potential for radiation accidents. Dr. Yamashita sends has summary of the "Diagnosis and Treatment of Radiation Injuries." The diagnostic procedures are about the same as have been previously mentioned. Concerning treatment for external irradiation, Dr. Yamashita writes:

> . . . If the exposure is very small and no changes found by blood examination, it would be permissible to let the patient go to his usual work, just avoiding overwork . . . if the exposure is fairly large and blood changes found, rest and suitable therapy must be given. Although for ordinary anemias blood transfusions are most effective and iron preparations are used with good response, these are not so effective for leukopenia due to radiation injury. The first in importance for treatment . . . is rest and nutrition . . . The preparations from liver and bone marrow are also said to be efficacious . . . It is considered that the drugs which stimulate the recticulo-endothelial system are effective. The administration of . . . Lumin, cobalt-chlorophyllin, Cepharatine, purified vaccine, etc., is done in Japan and is obtaining some effects . . . but these actions are not remarkable . . . Generally speaking, symptomatic treatments are very important. The avoidance of exhaustion of physical strength and the prevention of complications, such as bleeding and secondary infection, will greatly lower the danger of death.

Dr. Yamashita continues with a discussion of the treatment of internal irradiation:

> If it becomes clear that an isotope was inadvertently swallowed or inhaled . . . either gastric lavage or emetics . . . or purgatives must be used to bring quick elimination . . . The isotope adhering to the skin or a wound must be removed by washing off, using running water. Soap or acid clay is mostly used, and some organic solvent or oil is also useful in some cases . . . EDTA citrates or other chelates are said to be effective . . . The procedures to handle the internal irradiation from radioisotopes exceeding the maximum permissible level is about the same as in the case of external irradiation . . . As radiation injury lasts for a long time, even though its extent is slight, and as it sometimes gives rise to secondary changes, it is desirable to take preventive measures so as not to give rise to radiation injury . . . Being aware of the possibility (of various radiation accidents), counter plans must be laid out very prudently. Therefore, it is necessary not only to fear but to have a certain amount of knowledge concerning the diagnosis and treatment of all radiation injuries.

China

We do not know what is going on in Red China, but we do know that there were Co^{60} teletherapy machines and radioisotopes diagnosis and therapy going on as early as 1958. There are many nuclear reactors already in existence in China. Many people (including me) believe that they already have a nuclear weapon. They certainly have the trained personnel that would make a weapon possible.

In the Republic of China, on the Island of Taiwan, there is still considerable concern about relatively low levels of fallout radiation from the Russian, British and American nuclear testing. They still remember the "atomic-fish" from the Bikini test. There is considered to be no potentiality of a serious nuclear accident on the island except in the case of a nuclear war. However, the Tsing-Hua Nuclear Institute has already established a research reactor at Hsin-Chu. There are Co^{60} teletherapy machines and both industrial and medical use of radioisotopes, at least in Taipei.

Dr. Tien-Chenge Kao, Professor of Surgery and Superintendent of the National Taiwan University Hospital, writes concerning what their physicians will do about patients in the event of an accident:

> (1) Decontamination. At present only a few facilities can make a contamination survey of the patient. The National Taiwan University Hospital is the only civilian hospital that can do this, and, unfortunately, only on a limited scale. No decontamination facilities exist at present.
>
> (2) Medical care according to the type of injury.
>
> (3) Emergency rooms and special wards for the patient who has nuclear injuries should be constructed, but at the present, because of economy, the plan is still not realized.

Hong Kong

The Queen Mary Hospital in Hong Kong probably has the largest and most completely equipped radiology department in the Far East (outside of Japan). It has a number of large therapy accelerators, a well-equipped radioisotope laboratory, and a complete diagnostic service. Although Hong Kong does not maintain its own military force and thus probably will never have nuclear weapons, it is in the middle of a sensitive area. Dr. H. C. Ho writes concerning nuclear accidents as follows:

> (1) The potential for nuclear accidents in my area is nil for the near future. If an atomic or hydrogen bomb is dropped in Hong Kong, with 3,500,000 people crowded in a tiny area, it will be just "His Kingdom come" and nothing could be done about it because by then the few physicians which we have will perish together with the rest.
>
> (2) Treating the question theoretically, our physicians would deal with the patients according to what has been suggested in current books, reverse barrier nursing for those cases in which survival is possible, antibiotics to be withheld until there are signs of infection, platelet infusion for hemorrhagic states, and maintenance of fluids and electrolytes and nutrition.

India

V. W. Sivaramakrishnan is a Ph.D. biochemist, head of the Isotopes Division at the Cancer Institute in Madras, India. He has had considerable training both in America and in England and is very aware of the possibility of accidents.

NUCLEAR ACCIDENTS IN INDIA

V. M. Sivaramakrishnan, Ph.D.:

> The potential for nuclear accidents in India is very small but likely to increase. The Atomic Energy Establishments at Trombay, Bombay is the only "atomic" installation in India today. It is quite a large establishment containing three reactors, uranium and thorium processing plants, etc., and comparable in size and scope to the X-10 plants at Oak Ridge. An atomic reactor for power is under construction at Tarapore, a few hundred miles from Bombay, and there are proposals to have some more atomic power plants in the near future. Compared to its size and requirements, the power resources of India from conventional fuels are totally inadequate. Development of atomic power is an imperative necessity; nuclear industry, and hence nuclear accidents, have an important future.
>
> Radioisotopes are extensively used as tracers in a number of laboratories and industries. About a dozen hospitals use radioisotopes in internal medicine and have, in addition, kilocurie teletherapy units. A gamma-garden for botanical radiation research is functioning in Delhi. But a major nuclear accident occurring in any of these places is unlikely.
>
> There has not been any nuclear accident so far in India and the Indian physician will be confronted with a novel situation in the event of one occurring. Radiotherapists, in general, will probably fare better than the ordinary physician under these circumstances . . . Since there is no specific therapy as yet for nuclear injury, the treatment will be mainly symptomatic. Blood and bone marrow transfusions, administration of broad-spectrum antibiotics, bed rest, excellent nursing and continued observations are likely to play a vital part. The patient first must be classified according to the approximate extent of injury received and checked for radioactive contamination with the help of a health physicist.
>
> Bone marrow transfusion is not yet quite popular in Indian medical practice because the technique is still new here and the patient can suffer from the adverse results of immunological incompatibilities. Facilities for the treatment of burns are available in most of the Indian hospitals. The Safdharjung Hospital in New Delhi has a whole unit specializing on this subject.
>
> In the event of a peacetime nuclear accident, the government machinery is likely to step in and take charge as it did during the 1957 Asian Flu Epidemic. In a nuclear war (conjectured as global, of short duration and extensive), how much will be left for anyone to do anything with is purely a matter of speculation . . .

New Zealand

Everything in Atomic Energy can be traced back to Ernest Rutherford—a New Zealander. New Zealand is a small country whose main export seems to be giants in physics.

Dr. D. W. Urquhart, the radiotherapist at the Palmerston North Hospital in New Zealand, writes as follows:

> . . . My personal views do not necessarily represent the views of all of my colleagues . . . We have no reactor

in New Zealand. The safeguards for dealing with the usual type of nuclear accidents associated with medical or industrial use of large sources is taken care of in a way similar to that in other technologically advanced countries. Since 1949, we have had in operation a radiation protection legislation. All X-ray plants have had to be registered since 1944 and the types, amounts, location. methods of use, safeguards and waste-disposal arrangements of all radioactive substances within the country are under the strict control of one central laboratory, the Dominion X-ray and Radium Laboratory. This laboratory is a part of the Department of Health, and administers radiation protection legislation and provides, free of charge, assistance in radiation protection. Health Physics generally is required by holders of licenses to use radioactive substances. The possibility of nuclear accidents arising from warlike acts in New Zealand territorial waters cannot, of course, be reasonably assessed.

There has been no concerted effort as yet amongst the radiotherapists to formulate a plan of how to cope with the treatment of patients should a nuclear accident occur. Civil Defense Organization in this part of the world is still in its infancy, but the basic organization has been planned and I feel will in the near future call together medical men to formulate a concrete plan . . .

Australia

NUCLEAR ACCIDENTS

R. Rosen, Ph.D.*:

In the event of nuclear warfare, the population of Australasia is presumably less likely to be exposed in nuclear explosions than the population of the northern hemisphere; but neither group will escape from exposure to the long-lived fission products. Although planning for such exigencies has commenced, planning for radiation accidents unrelated to warfare must not be neglected.

Medical practitioners will want to be informed of the surprising extent to which potentially dangerous radiation is already employed for peaceful purposes in advanced communities. The number and variety of these applications are increasing rapidly, and the planning of appropriate health and safety programs is needed. This will in turn contribute to a large degree to the effectiveness of Civil Defense in the event of nuclear warfare . . .

The specialty of health physics has become firmly established. Planning for radiation accident situations should be carried out jointly by physicians and health physicists . . . The proper management of accident victims will depend on prior diagnosis. The accuracy with which this can be made will depend on the degree to which the dosage distribution and other characteristics of the radiation are known. It will also require a proper knowledge of the characteristics of the absorbing biological media and of their metabolic processes . . .

It is quite likely that biological cells and tissues have always suffered effects from low level radiation processes. Thus the clinical effects of man-made radiation are not caused by wholly new etiological agents. The new features are the greater degree of damage and the larger number of victims.

Planning of modern radiation facilities involves provision for adequate preventive and protective equipment. Where one of the deficiencies in safety control is a program dealing with radiation accident situations, planning should be directed to applying first aid, decontamination and transportation for the victim, and to providing reception stations and staff adequately prepared for the isolation and treatment of these persons. Analysis of the accident should be carried out early so that the victims may benefit from as full a knowledge of the dosimetry as possible. Education and public relations services should be organized to avoid adverse sociological effects within the community, to give reassurance, and so that the community will know that the emergency service is available and how and when to call upon it.

The accident-free record of radiation workers is quite good, due in part to their realization of their responsibilities and the high degree of care required of them. But the increase in radiation devices in so many technical fields emphasizes the need for planning.

In Australasia there exist, already, radiation facilities comparable to those in other regions, even including reactors. These facilities are no less capable of inflicting disastrous injury than are similar facilities elsewhere. Accidents arising from them could produce injuries of greater severity to their victims than might be expected from fallout. Thus the same problem exists in Australasia as exists in the United States, but for the moment it appears to be of lesser degree.

The Rest Of The World

It is unnecessary to detail the entire world country by country. Both radiation and radioactivity were discovered on the continent of Europe. The U.S., U.S.S.R., England, France and China already have atomic weapons. The U. S. alone has about 25,000 "tactical" (less than one kiloton) warheads and about 7,000 to 10,000 large (megaton range) warheads Canada, Japan, Israel, India, a number of Scandinavian, European and British Commonwealth countries, probably even Egypt, could produce them on about a year's notice. There is no secret.

There are between 250 and 300 reactors in the United States; about the same number are in operation or are being planned in other countries. There are almost 1600 large teletherapy installations through the Western world. (We don't know what's going on behind the Iron Curtain, but we can assume about half of what is in the Western countries.) There are at least 500 large accelerators and about 50 other multikilocurie radioisotope sources, about 1,000 therapeutic X-ray machines and about 10,000 diagnostic machines. Between 10,000 and 100,000 patients are being treated with radioisotopes annually; the diagnostic doses probably come close to a million annually. If it were uncontrolled (it is highly controlled and very safely handled), there is enough reactor waste being produced to poison the oceans. The extraordinary safety record of the Atomic Energy Industry in the past has been due to meticulous precautions.

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* Radiation Protection Officer The University of New South Wales, Kensington, Australia.

But accidents will happen. The odds of dealing a perfect contract bridge hand are said to be about one in 600 billion; the odds of all four players being dealt a perfect hand on the same deal are infinitesimal. On August 11, 1963 the Associated Press reported such an occurrence. We can predict with absolute certainty that any physician now alive will ultimately die; we don't know what the odds are for his taking care of a radiation accident while alive, but they are growing.

On Science And Culture

In traditional societies, the great function of culture is to keep things rather stable, quiet, and unchanging. It has been the function of tradition to assimilate one epoch to another, one episode to another, even one year to another. It has been the function of culture to bring out meaning, by pointing to the constant or recurrent traits of human life, which in easier days one talked about as the eternal verities.

In the most primitive societies, if one believes the anthropologists, the principal function of ritual, religion, of culture is, in fact, almost to stop change. It is to provide for the social organism what life provides in such a magic way for living organisms, a kind of homeostasis, an ability to remain intact, to respond only very little to the obvious convulsions and alterations in the world around.

Today, culture and tradition have assumed a very different intellectual and social purpose. The principal function of the most vital and living traditions today is precisely to provide the instruments of rapid change. There are many things which go together to bring about this alteration in man's life; but probably the decisive one is science itself. I will use that word as broadly as I know, meaning the natural sciences, meaning the historical sciences, meaning all those matters on which men can converse objectively with each other. . . . When we talk about science today, we are likely to think of the biologist with his microscope or the physicist with his cyclotron; but almost certainly a great deal that is not now the subject of successful study will later come to be. I think we probably today have under cultivation only a small part of the terrain which will be natural for the sciences a century from now. I think of the enormously rapid growth in many parts of biology, and of the fact, ominous but not without hope, that man is a part of nature and very open to study.

The reason for this great change from a slowly moving, almost static world, to the world we live in, is the cumulative character, the firmness, the givenness of what has been learned about nature. . . . Thus everything that is found out is added to what was known before, enriches it, and does not have to be done over again. This essentially cumulative irreversible character of learning things is the hallmark of science.—J. Robert Oppenheimer. "On Science and Culture." *Encounter,* October, 1962, p. 3.

VII. Sources OF Information

An Annotated Bibliography On The Radiation Accident Problem

Marshall Brucer, M.D.

■ The field of Nuclear Medicine covers not only all of medicine, but all of science; in fact, to be a real expert (as in every other field) one should know everything. In application, a total knowledge is seldom necessary but, especially after a radiation accident, it is desirable to explore each topic. This annotated bibliography is divided into eight major facets, only briefly covered in the text. These are sources of information; bibliographic references are contained within the body of the text.

Each of the eight major sections is subdivided into three classifications—*Introductory, Intermediate,* and *Advanced.* The Introductory books are usually general statements of the problem. The Intermediate documents are within the scope of the usual training of physicians. The Advanced statements are usually definitive. They may not be written for physicians.

I. Basic Radiation Physics

A. INTRODUCTORY

1. Romer, A.
   The Restless Atom.
   SCIENCE STUDY SERIES S 12, Anchor Books
   Garden City, New York, Doubleday, 1960.
2. Pollard, E. C. and Davidson, W. L.
   APPLIED NUCLEAR PHYSICS, 2nd ed.
   New York, John Wiley, 1951.
3. Andrews, H. L.
   RADIATION BIOPHYSICS.
   Englewood Cliffs, New Jersey, Prentice-Hall, 1961.

B. INTERMEDIATE

1. Glasstone, S.
   SOURCEBOOK ON ATOMIC ENERGY, 2nd ed.
   Princeton, New Jersey, D. Van Nostrand, 1958.
2. Glasser, O., editor
   MEDICAL PHYSICS, Volumes I, II, III.
   Chicago, Year Book Publishers, 1960.
3. Mayneord, W. V.
   SOME APPLICATIONS OF NUCLEAR PHYSICS TO MEDICINE.
   Brit. J. Radiol., Supplement No. 2, 1950, 290 pp.

C. ADVANCED

1. Compton, A. H. and Allison, S. K.
   X-RAY IN THEORY AND EXPERIMENT, 2nd ed.
   New York, D. Van Nostrand, 1935.
2. Evans, R. D.
   THE ATOMIC NUCLEUS.
   New York, McGraw-Hill, 1955.
3. Hines, G. J. and Brownell, G. L.
   RADIATION DOSIMETRY.
   New York, Academic Press, 1956.

It is impossible to understand radiation accidents unless one understands a minimum of nuclear physics. Romer's *The Restless Atom* is a historical, almost storybook treatment of how radioisotopes were first discovered. During the interesting period after the turn of the century, the complex interrelationships of the natural radioisotopes were first worked out. The Pollard-Davidson text is built around radioisotopes, how they are made, what they do, how the radiation is produced. It was not written for physicians, but at the intellectual level of a graduate in an entirely different field of science. The Andrews text on *Radiation Biophysics* is a concise, simplified statement of the whole material covered in the Pollard-Davidson and Romer texts but relates the application to biological and human problems.

The Glasstone Intermediate text is an encyclopedic coverage of the field of nuclear energy; the physics segments are superlative, the medical segments are naive. The Glasser text is a series of many biophysical subjects as they relate directly to medical problems. The Mayneord document is concerned neither with the Glasstone pure physics nor the Glasser medical physics, but with specific applications of radiation and its concomitants in clinical problems. These three texts together are probably definitive as far as physicians are concerned, but not for physicists.

The three Advanced texts, advanced even for physicists, are classics in the field. All three are written by physicists for physicists with advanced degrees and make no attempt to explain or to simplify. There is no compromise with the problem of teaching physicians who do not have extensive training in physics.

II. Health Physics Manuals And Expositions

A. INTRODUCTORY

1. Brannigan, Francis L.
   RADIATION SAFETY PRIMER, 2nd ed., revised, 1963.
   LIVING WITH RADIATION: THE PROBLEMS OF THE NUCLEAR AGE FOR THE LAYMAN.
   United States Atomic Energy Commission, Safety and Fire Protection Branch, Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C. 1959.
2. U. S. Navy, many authors.
   PRINCIPLES OF RADIATION AND CONTAMINATION CONTROL.
   Vol. 1, Radsafe for Everybody; Vol. 2, Procedures and Guidelines Relating to Nuclear Weapon Effects; Vol. 3, Technical Information Relating to Nuclear Weapons Effects.
   Prepared by the personnel at the U. S. Naval Radiological Defense Laboratory, San Francisco, Published by the Bureau of Ships, Navy Department, Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. NAVSHIPS 250-341-3.

B. INTERMEDIATE

1. Blatz, H., Editor
   RADIATION HYGIENE HANDBOOK.
   New York, McGraw-Hill, 1959.
2. Drummer, J. E., Jr., Compiler and Editor
   GENERAL HANDBOOK FOR RADIATION MONITORING.
   United States Atomic Energy Commission Report LA-1835 (3rd ed.) 1959.
   Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C.

C. ADVANCED

1. I C R P, many authors
   RECOMMENDATIONS OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, I, II, III.
   London, Pergamon Press, Ltd., 1958-1960.
2. U. S. Congress, many authors
   THE NATURE OF RADIOACTIVE FALLOUT AND ITS EFFECTS ON MAN.
   Hearings before the Special Subcommittee on Radiation of the Joint Committee on Atomic Energy, Congress of the United States, Eighty-fifth Congress, parts 1-3.
   U. S. Government Printing Office, Washington 25, D. C., 1957.

The subject of health physics is not so important as hysterical government headline writers would have you believe; but it is related to legalistic restrictions. Very large amounts of radiation endanger personnel; small amounts of radiation endanger instruments.

The three Introductory references are truly introductory. *Living with Radiation* is divided into two parts; one part is the series of slides that can be furnished by the AEC Health and Safety Branch; the second part is a written statement. The two together are suitable for presentation to completely untrained personnel. The second document was published by the United States Navy for its own personnel. It is in three volumes: first, an elementary statement of principles; second, the techniques for technicians who must do monitoring; third, the reasons for these monitoring procedures.

The Intermediate documents on health physics make little attempt to explain the principles of action, but they give the actual methods that have been and are being used.

The Advanced texts are definitive statements on problems most worrisome in radiological protections. The ICRP statement covers an international committee's recommendations (used by almost every political body.) This document has been interpreted and reinterpreted in almost every other health physics text. The Congressional Hearings on fallout consider all the problems related to the use of radiation under almost any circumstance. The hearings themselves are not very important, but included are reprints of many of the original documents that led to the opinions we now hold.

III. Compilations Of Data

A. INTRODUCTORY

1. Slack, L. and Way, K.
   RADIATIONS FROM RADIOACTIVE ATOMS IN FREQUENT USE.
   United States Atomic Energy Commission, U. S. Government Printing Office, Washington 25, D.C., 1959.
2. Sullivan, W. H.
   TRILINEAR CHART OF NUCLIDES
   United States Atomic Energy Commission, 2nd ed., January 1957.
   Revision sheets by subscription.
   Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C.

B. INTERMEDIATE

1. National Bureau of Standards Handbooks, No. 42, 48, 49, 50, 51, 53, 57, 58, 59, 63, 65, 66, 69, 72, 73, 75, 76, 77 (Vol. III), 78, 79, 80, etc.
   U. S. Government Printing Office, Washington 25, D. C., many dates and revisions.

2. RADIOLOGICAL HEALTH HANDBOOK.
   Compiled and edited by Division of Radiological Health. Revised ed., 1960. U. S. Department of Health, Education and Welfare, Public Health Service.
   Office of Technical Services, Department of Commerce, Washington 25, D. C. (PB 121784).

C. ADVANCED

1. NUCLEAR DATA TABLES 1960, Parts 1-3. U. S. Government Printing Office, Washington 25, D. C.
2. Strominger, D., Hollander, J. M. and Seaborg, G. T.
   TABLE OF ISOTOPES.
   Revs. Modern Phys. 30: No. 2, Part 2, 585-904, 1958.
3. Way, K., King, R. W., McGinnis, C. L. and von Lieshout, C. L.
   NUCLEAR LEVEL SCHEMES.
   National Academy of Sciences—National Research Council. Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

More than a thousand different radioisotopes have been discovered. Of these, 276 have a direct medical interest. There is an ever-growing number of isomeric states. Sometimes these isomers are more important than the parent radioisotopes, especially as far as dosimetry is concerned. No one can remember all the half-lives, energy levels, or types of radiations. Thus, there must be a series of tables of data.

The two Introductory texts are not introductory in that their data are less advanced. They are introductory in the sense that they "make a decision" and present only one side of the story. The Slack and Way compilation selects only a few commonly used medical radioisotopes, makes a decision on which are the best data (the authors admit that this might not be true) and then present them in detail. The Sullivan *Trilinear Chart* was not made for physicians. It attempts to take all the data on all the isotopes and to arrange them in a systematic fashion so that any person can easily find and compare one isotope with another. Dr. Sullivan has made a decision on which data are "best." This compilation was kept up to date (to 1963).

The Intermediate documents are neither compilations of data nor are they texts on how to use data; they are a combination of the two. The National Bureau of Standards Handbooks are interpretations of specific topics. They are semi-official, represent a committee compromise, and are quasi-legally authoritative.

The Advanced compilations of data make no choice between documents. They present all the data. There has been some selection, but this is based upon an expert physicist's (or chemist's) interpretation of an experiment. Instead of using the words "Introductory," "Intermediate," and "Advanced," in this particular series of compilations, it probably would have been better to use the words, "Selected," "Interpretive," and "Complete."

IV. Instrumentation

A. INTRODUCTORY

1. Morris, A. C., Jr.
   A PHYSICIAN'S INTRODUCTION TO ELECTRONICS.
   London, Pergamon Press, Ltd., 1961
2. Ross, D. A.
   MEDICAL GAMMA-RAY SPECTROMETRY, bound with Harris, C.C., Hamblen, D. P. and Francis, J. E.
   BASIC PRINCIPLES OF SCINTILLATION COUNTING FOR MEDICAL INVESTIGATORS.
   United States Atomic Energy Commission Report ORNL-30, 1959.
   Office of Technical Services, Department of Commerce, Washington 25, D. C., 1959.
3. Upton, M.
   ELECTRONICS FOR EVERYONE.
   New York, Signet Key Books, The American Library of World Literature, 1957, or New York, Devon-Adair, 1954, 2nd ed., 1962.

B. INTERMEDIATE

1. Brucer, M.
   RADIOISOTOPE SCANNING.
   United States Atomic Energy Commission Report ORINS-20, 1958.
   Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C., 1958.
2. Brucer, M.
   THYROID RADIOIODINE UPTAKE MEASUREMENT. A Standard System for Universal Intercalibration.
   United States Atomic Energy Commission Report ORINS-19, 1959.
   Office of Technical Services, Department of Commerce, Washington 25, D. C., 1959.
3. Price, William J.
   NUCLEAR RADIATION DETECTION.
   New York, McGraw-Hill, 1958.

C. ADVANCED

1. Bell, C. G., Jr. and Hayes, F. N.
   LIQUID SCINTILLATION COUNTING.
   London, Pergamon Press, Ltd., 1958.

2. Siegbahn, K., Editor
   BETA- AND GAMMA-RAY SPECTROSCOPY.
   New York, Interscience Publishers, 1955.
3. Strobel, H. A.
   CHEMICAL INSTRUMENTATION.
   A Systematic Approach to Instrumental Analysis.
   Reading, Massachusetts, Addison-Wesley, 1960.

When radioisotopes are used, fiddling with, adjusting, and attempting to understand instruments takes the major portion of any physician's time. Most of his decisions will ultimately depend upon the workings of an electronics instrument.

It is not necessary for a physician to know electronics, but he must understand the basic terms. The Morris document describes terms built around a highly simplified first approach. A breadboard of electronic devices was built for the teaching of physicians who are already experts in pathology but not experts in electronics. The Ross and Harris documents describe in detail one kind of a detector, the crystal spectrometer. This has been emphasized because scintillation counting has become the most common medical tool for radiation detection. The Upton text is an inexpensive paperback that was sold to the general public to describe television tubes and radio receivers. In the process of making this description, the use of tubes and wires, resistors and capacitors is explained to persons who might never look inside the chasis of a counting system but must understand that something logical is happening.

The Intermediate texts are explanatory of an external measurement, and gamma rays. The third is built around the entire field, particularly the detection of nonelectromagnetic radiation. These are Introductory texts, but they are Intermediate in the sense that they specify problems.

The three Advanced texts are definitive, written by and for experts. One describes only liquid scintillation detection. Another describes all kinds of scintillation detection, particularly as it relates to the very important separation of one energy from another. The Strobel text covers all kinds of instrumentation, most of which ultimately finds a usefulness in medicine.

V. Radiation Biology

A. INTRODUCTORY

1. Henry, H. F.
   IS ALL NUCLEAR RADIATION HARMFUL?
   United States Atomic Energy Commission Report K-1470, 1961.
   JAMA 176: 671-675, 1961. (A condensation of K-1470).
2. Kaplan, I. I.
   GENETIC EFFECTS IN CHILDREN AND GRANDCHILDREN, OF WOMEN TREATED FOR INFERTILITY AND STERILITY BY ROENTGEN THERAPY.
   Radiology 72: 518-521, 1959.
3. Simon, N., Brucer, M. and Hayes, R. L.
   RADIATION AND LEUKEMIA IN CARCINOMA OF THE CERVIX.
   Radiology 74: 905-911, 1960.

B. INTERMEDIATE

1. Neel, J. V .and Schull, W. J.
   THE EFFECT OF EXPOSURE TO THE ATOM BOMBS ON PREGNANCY DETERMINATION IN HIROSHIMA AND NAGASAKI.
   Washington, D.C., National Academy of Sciences—National Research Council, 1956 (Publication No. 461).
2. Glasstone, S.
   THE EFFECTS OF NUCLEAR WEAPONS, Revised edition.
   U.S. Department of Defense, U.S. Atomic Energy Commission,
   Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C., April 1962.

C. ADVANCED

1. Many authors.
   Many titles, related to radiation effects, both somatic and genetic.
   Published papers of the Atom Bomb Casualty Commission (ABCC): Numbered technical reports (the first two numbers are report numbers, the last two numbers are the year). In English and in Japanese.
   National Academy of Sciences — National Research Council, 1957-58-59-60-61-62-63-.
2. Many authors.
   RADIOBIOLOGY: Experimental and Applied.
   Brit Med Bull 4:1-73, 1946.
3. Ellinger, F.
   MEDICAL RADIATION BIOLOGY.
   Springfield, Illinois, Charles C Thomas, 1957.

Thousands of textbooks and articles and even a number of societies are devoted to radiation biology. Few of these have anything to do with the human problem. Many of the important radiobiological problems (lifespan, genetic effects, leukemia, carcinogenesis) have become sounding boards for political propaganda. A substandard class of scientists has gravitated into the field and the deluge of verbose texts, papers and "scientific projects" attests to the scientific buggy ride that is being perpetrated.

The three Introductory references are on specific problems. In a sense they are debunking reviews of literature. The Henry article debunks the harmfulness of low-level radiation by pointing out that most of the experiments have found no effects. The Kaplan article debunks the genetic effects by pointing that even with fairly large therapeutic doses of radiation genetic effects do not occur. The Simon article debunks the "certainty" of leukemia following total-body irradiation.

The Intermediate texts are more complete reviews. Neel and Schull summarize most of the exposure data during pregnancy in the two large population exposures that have occurred. The Glasstone *Effects of Nuclear Weapons* is a semi-official statement on Blast, Burn, and Radiation. It was thoroughly reviewed, criticized and revised before publication. It is not only authoritative, but it is interesting reading.

The Advanced texts are definitive in their field. The Atom Bomb Casualty Commission Reports (published in English and Japanese) illustrate the results of an uncontrolled study, but it is as complete a study as may ever be made concerning radiation effects. There are many titles. Most are statements on small subsubjects. The British Medical Bulletin published a symposium on radiobiology, which includes many authors all of whom are experts in their own fields. The Ellinger text reviews almost everything in radiation biology (medical and nonmedical); about a third of the book is a list of references.

VI. Laboratory Methods And Guides

A. INTRODUCTORY

1. Faires, R. A. and Parks, B. H.
   RADIOISOTOPE LABORATORY TECHNIQUES.
   London, George Newnes, 1958.

B. INTERMEDIATE

1. Danforth, J. P. and Stapp, R. D., editors.
   RADIOISOTOPES IN INDUSTRY. TRAINING PROGRAM.
   Vol. I and II.
   General Motors Institute, Flint, Michigan.
   Paperbound from the Office of Technical Services, Department of Commerce, Washington, 25, D.C., 1959.

C. ADVANCED

1. Overman, R. T. and Clark, H. M.
   RADIOISOTOPE TECHNIQUES.
   New York, McGraw-Hill, 1960.

There is no good laboratory manual for guidance in medical radioisotope techniques. The Faires and Parks text is an introductory guide only in the sense that it talks from the standpoint of laboratory methods. The Danforth and Stapp volumes are the General Motors Institute Training Guides. They contain pictures, diagrams, references, questions, and describe in great detail all the methods that are used with radioisotopes in industrial situations. In the sense that the movement of blood through a vessel is the same as the movement of water through a pipe, the principles of the technique are similar. Eventually, something like this General Motors Training Guide will be done in the field of medicine.

The Overman and Clark *Radioisotope Techniques* book is not a simple book to read for a person untrained in advanced chemistry. However, most medical radioisotope measurements are a kind of chemical manipulation.

VII. Nuclear Medicine Texts

A. INTRODUCTORY

1. Fields, T. and Seed, L., editors.
   CLINICAL USE OF RADIOISOTOPES.
   A manual of technique, 2nd ed.
   Chicago, Year Book Publishers, 1961.

B. INTERMEDIATE

1. Beierwaltes, W. H., Johnson, P. C. and Solari, A. J.
   CLINICAL USE OF RADIOISOTOPES.
   Philadelphia, Saunders, 1957.

C. ADVANCED

1. Many authors.
   ISOTOPES IN MEDICINE.
   Brit Med Bull 8:115-255, 1952.

The Fields and Seed text on the *Clinical Use of Radioisotopes* is not a manual of techniques as is stated in the subtitle. It is an introductory explanation of how certain clinical tests are done. The Beierwaltes text is a clinical examination of radioisotope techniques with a physiological explanation of the methods. This is the most complete and authoritative single medical statement on the use of radioisotopes. (It is now undergoing revision). The *Isotopes in Medicine* summary of many subjects by many authors is an advanced text on specific topics. It has a chemical rather than a radiological bias. These are a series of papers rather than a textbook covering the entire field; much of the instrumentation (but none of the ideas) is out of date.

VIII. Radiation Accidents (The Medical Problems)

A. INTRODUCTORY

1. Saenger, E. L., editor
   MEDICAL ASPECTS OF RADIATION ACCIDENTS.
   A handbook for physicians, health physicists, and industrial hygienists.
   General Hospital, Cincinnati, USAEC, Reviewed from final draft manuscript, 1961.

B. INTERMEDIATE

1. Many authors, no editor announced.
   Scientific Meeting on the Diagnosis and Treatment of Acute Radiation Injury, Geneva, 1960.
   DIAGNOSIS AND TREATMENT OF ACUTE RADIATION INJURY; proceedings of a scientific meeting jointly sponsored by the World Health Organization and the IAEA.
   U.S. ed. New York, International Documents Service, 1961.
2. Leroy, G. V., Chairman of Subcommittee.
   EXPOSURE TO IRRADIATION IN AN EMERGENCY.
   Recommendations of the National Committee on Radiation Protection and Measurement.
   Report No. 29, available from the Department of Nuclear Medicine, Department of Pharmacology, University of Chicago, June 1962.

C. ADVANCED

1. Hemplemann, L. H., Lisco, H. and Hoffman, J. G.
   THE ACUTE RADIATION SYNDROME: A STUDY OF NINE CASES AND A REVIEW OF THE PROBLEM.
   Ann. Int. Med. 36: 279-510, 1952. (Feb.) No. 2, pt. 1.
2. Graham, T. E.
   MEDICAL MEMORANDUM ON CRITICALITY.
   Medical Department, Windscale Works, United Kingdom Atomic Energy Authority.
   Mimeographed (formerly labeled confidential) 20 June 1956.
3. Brucer, M., editor
   THE ACUTE RADIATION SYNDROME.
   U.S. Atomic Energy Commission USAEC Report ORINS-25, 1959.
   Technical Information Service, Department of Commerce, Washington 25, D.C.
4. Cronkite, E. P. and Bond, V. P.
   RADIATION INJURY IN MAN: ITS CHEMICAL AND BIOLOGICAL BASIS, PATHOGENESIS AND THERAPY.
   Springfield, Illinois, Charles C Thomas, 1960.
5. Shipman, T. L., compiler.
   ACUTE RADIATION DEATHS RESULTING FROM AN ACCIDENTAL NUCLEAR CRITICAL EXCURSION.
   J Occup Med 3 (3): Special Supplement, March 1961.

There is no reliable introductory text for nonphysicians. The Saenger text assumes considerable medical knowledge and is Introductory only in that it briefly covers the entire nonmedical as well as the medical field.

The World Health Organization (with the IAEA) held a symposium in 1960 reviewing many of the early accidents (some are summarized). The University of Chicago section of Nuclear Medicine in the Department of Pharmacology has gathered a semiofficial subcommittee on the National Committee on Radiation Protection and Measurement to discuss the safety problems involved in nuclear accidents. The proceedings have been published as an NBS Handbook. Without regard to the innumerable questions raised (both medical and physical), the handbook authoritatively summarizes the entire health physics field in regard to accidents as of 1961.

The Advanced texts are both historical and definitive. The Hemplemann article is probably the initial complete statement on the medical problems of the first recognized nuclear accident. The Graham text is the first development of the problem as it might affect an industrial complex. It foresees many of the problems that later occurred. The last three documents are by Oak Ridge authors after an Oak Ridge accident, by Brookhaven authors after a severe accident of fallout in the South Pacific, and by Los Alamos authors after a serious reactor-processing malfunction. Each of these represents a different approach to the therapy of accidents, but all with about the same conclusions. All three are based on interpretations of accidents for which the authors had medical responsibilities.

THE PRESIDENT'S PAGE

C.M.S. — A Re-appraisal

At this writing, the situation existing between the Connecticut State Medical Society and Connecticut Medical Service remains at an impasse. Dates for liaison meetings have not yet been set, nor can we do more than surmise what the outcome will be.

Quite naturally the aims of the two organizations are diverse. The Medical Society represents physicians who have services to offer, while C.M.S. is a salesman of these services. The conflict arises as to how much of their service members of the Medical Society wish to offer, while C.M.S. drives for ever more service to sell.

Although past reviews of the origins of a supposed CMS-CSMS agreement have shed little light on the subject, the origins cannot be ignored entirely if one is to make any sense of the present conflict. In 1948, the C.S.M.S. agreed to urge its members to provide services at greatly reduced fees so that those with reduced incomes could be guaranteed adequate medical care through CMS. In order to assure the success of the new venture, the Society agreed to serve as sponsor for C.M.S., and encouraged a large enough number of its members to become participating physicians to satisfy the requirements of the Insurance Commissioner. Thus success of the venture was assured.

In 1948, C.M.S. consented to the conditions offered by C.S.M.S. and no one can deny that the plan has prospered mightily under the arrangement. Apparently there's the rub — as has been pointed out by its management, an organization cannot stand still. If it does not progress it regresses. Who can blame the management then, for doing everything in its power to further the scope of so successful an enterprise as C.M.S.?

The Medical Society recognizes that much of the success of C.M.S. has been at the expense of the membership of C.S.M.S., and is fearful that further C.M.S. expansion will be at increased expense to the membership of C.S.M.S. It points to visible evidences of the success of C.M.S.; i.e., the splendid buildings and the splendid surplus. It is concerned lest fixed fee schedules which have been intended to be reduced fees for the benefit of C.M.S., members may actually become total fees applicable to all patients.

The Medical Society is aware of the growing trend for total coverage by insurance of medical expenses, but considers it difficult to achieve when one considers the different types of coverage needed in rural, suburban and urban areas of the state. It has yet to learn of a truly successful method of universal coverage.

From the viewpoint of C.M.S., many difficulties are being encountered despite the advantage offered by service benefits. C.M.S. finds itself in keen competition with other insurance companies in the state. It is alleged that the influence of the Society, as sponsor, has sometimes resulted in limiting what it has to offer in the way of desirable contracts to such a degree that it loses opportunities to increase its membership. Certainly this has been the paramount influence in the current conflict.

C.M.S. is now a multimillion dollar corporation, with many responsibilities, not only to its membership, but to the physicians of Connecticut as well. Its relationship to the State Society has become unwieldly and I am certain its Board of Directors has for a long time considered State Society sponsorship of waning value. Perhaps the time has come for both parties involved in the conflict to face the issue squarely. Does C.M.S. truly need C.S.M.S. sponsorship? Does C.S.M.S. wish to continue its association with what has become a highly competitive insurance business? These are the questions to be considered, and soon.

Morris P. Pitock, M.D.

172nd ANNUAL MEETING

of the

CONNECTICUT STATE MEDICAL SOCIETY

Statler-Hilton Hotel

10 Ford Street, Hartford, Connecticut

April 28, 29, 30, 1964

PROGRAM COMMITTEE

Allen M. Margold, *Norwalk, Chairman*

Peter J. Scafarello, *Hartford*

Paul F. McAlenney, Jr., *New Haven*

MESSAGE FROM THE PRESIDENT

Another Spring is upon us, and April is the month which brings with it the 1964 annual meeting of the Connecticut State Medical Society. It will be the 172nd such affair and, as your retiring president, I wish to greet you warmly and express my personal hope that each of you will make a special effort to participate in both the medical and social activities of this year's Scientific Assembly. The Program Committee has put together a series of excellent presentations by well-known speakers, there will be many interesting exhibits to command your attention, and the annual dinner promises to be an outstanding one. I look forward to seeing you in attendance at this important function of the Society which marks the end of my term of office.

Morris P. Pitock, M.D.

GENERAL INFORMATION

Read Carefully

REGISTRATION:

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

PARKING:

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

TELEPHONE:

Telephone messages will be received at Hartford 249-5611.

LUNCHEONS:

Luncheons will be served in the City Rooms on the Mezzanine on April 29 and 30 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUESTS OF THE SOCIETY. PLEASE REMEMBER, A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

HOTEL ACCOMMODATIONS:

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society Meeting. Your letter should be directed to the Front Office Manager, Statler-Hilton Hotel, 10 Ford Street, Hartford 3, Connecticut. Special reservation cards are available in the Society office and will be mailed to members upon request.

ANNUAL DINNER:

The Annual Dinner will be held at the hotel on Wednesday, April 29, 1964. The social hour will be at 6:15 P.M. and the dinner at 7:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promply* at 6:15 P.M. and end *promptly* at 7:00 P.M. Your reservation for dinner should be sent in as soon as possible.

PROGRAM:

General scientific sessions will be held in the terrace room from 9:30 A.M. to 3:30 P.M. Section meetings will begin at 3:30 P.M. and will be held in the rooms listed in the program.

EXHIBITS:

The technical exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review, "under one roof" what is new and timely in the goods and services available to the Connecticut physician.

PROGRAM

Tuesday April 28

MEZZANINE

Annual Meeting of the House of Delegates

MICHAEL R. SCULLY, *Bridgeport, Speaker of the House, presiding*

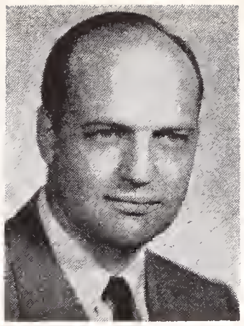
10:00 CALL TO ORDER
BUSINESS SESSION

1:00 LUNCHEON FOR OFFICERS, MEMBERS OF THE HOUSE AND GUESTS

2:00 RESUMPTION OF BUSINESS
Social hour immediately following the adjournment of the meeting.

CHESTER S. KEFFER
Boston, Massachusetts

LOUIS WEINSTEIN
Boston, Massachusetts


JOHN H. MOYER
Philadelphia, Pa.

Wednesday, April 29

9:00 REGISTRATION—MEZZANINE

TERRACE ROOM

9:30 CALL TO ORDER—Ralph L. Gilman, Storrs, President of the Society
ADDRESS OF WELCOME—Kenneth F. Brandon, President, Hartford County Medical Association

ALLEN M. MARGOLD, *Norwalk, presiding*

9:45 FEVER—ITS DIAGNOSTIC SIGNIFICANCE
CHESTER SCOTT KEEFER, *Boston; Professor of Medicine, Emeritus, Boston University; Consultant in Medicine, Massachusetts Memorial Hospitals*

10:30 RECENT ADVANCES IN THE TREATMENT OF INFECTION
LOUIS WEINSTEIN, *Boston; Professor of Medicine, Tufts University School of Medicine; Associate Physician-in-Chief and Chief of the Infectious Disease Service, Pratt Clinic—New England Center Hospital*

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 MEDICAL ASPECTS OF RENAL HYPERTENSION
JOHN H. MOYER, III, *Philadelphia; Professor and Chairman, Department of Medicine, Hahnemann Medical College and Hospital*

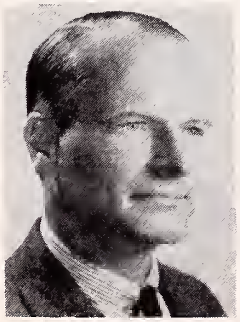
12:20 PHEOCHROMOCYTOMA
OLIVER COPE, *Boston; Professor of Surgery, Harvard Medical School; Visiting Surgeon, Massachusetts General Hospital*

1:00 LUNCHEON—CITY ROOMS
INTERMISSION TO VISIT TECHNICAL EXHIBITS

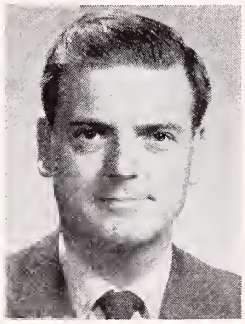
PAUL F. MCALENNEY, JR., *New Haven, presiding*

2:00 TRAGEDY OF THE WASP STING
MARY H. LOVELESS, *New York City; Associate Professor of Clinical Medicine, Cornell University Medical College; Assistant Attending Physician to Outpatients, New York Hospital*

2:40 THE PRACTICAL MECHANICS OF MANAGING ALLERGIC PATIENTS IN THE PRIVATE PRACTICE OF PHYSICIANS WHO ARE NOT ALLERGICALLY TRAINED
DOUGLAS E. JOHNSTONE, *Rochester, New York; Clinical Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Director of Pediatric Allergy Clinic, Strong Memorial Hospital*


OLIVER COPE
Boston, Massachusetts

MARY H. LOVELESS
New York City


DOUGLAS E. JOHNSTONE
Rochester, New York

Wednesday, April 29

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY

20th Annual Meeting — Tumble Brook Country Club, Bloomfield

President: Mrs. Fritz Meyer, Bridgeport
Recording Secretary: Mrs. Forrest D. Gibson, *Farmington*
Corresponding Secretary: Mrs. Nicholas E. Creaturo, *Trumbull*

10:00 Registration

10:30 Business Meeting

12:00 Hospitality Hour and Fashion Show

1:00 Luncheon

Guest Speaker

William B. Walsh, m.d., *Washington, D.C., Founder and President of the "Project Hope"*

SECTION ON DERMATOLOGY

3:30 Room 424

President: Frank M. Castiglione, *New Haven*
Secretary: Patrick N. Brown, *Meriden*

Acne Vulgaris—Its Pathodynamics and Relationship to Treatment

John S. Strauss, *Boston; Associate Professor of Dermatology, Boston University School of Medicine; Associate Attending, Massachusetts Memorial Hospitals, Boston; Consultant at Lemuel Shattuck Hospital, Framingham*

SECTION ON GASTROENTEROLOGY

4:30 Rooms 416-420

President: Frank K. Abbot, *Waterbury*
Secretary: Vincent A. DeLuca, Jr., *Derby*

Clinical Application of Radio Isotopes in the Differential Diagnosis of Liver Disease

Nilo E. Herrara, *Danbury; Assistant Clinical Professor of Pathology, Yale University School of Medicine; Chief of Pathology, Danbury Hospital*

Raphael D. Schwartz, *Danbury; Attending in Medicine, Danbury Hospital; Instructor in Medicine, Yale University School of Medicine*

SECTION ON INTERNAL MEDICINE

3:00 Rooms 416-420

President: Daniel B. Hardenbergh, *Southport*
Secretary: Robert J. Molloy, *Hartford*

Morris J. Seide, *Hartford, presiding*

The Medical Biopsy: A Neglected Diagnostic Tool for the Physician

Bone Marrow Biopsy—Norma Granville, Hartford
Comments by Stuart Finch, New Haven

G-I Biopsy—Robert Rossen, Hartford
Comments by Walter Thayer, New Haven

Pleural Biopsy—Stephen B. Sulavik, New Haven
Comments by Nicholas Marinaro, Newington

Kidney Biopsy—Mark W. Izard, Hartford

Wednesday, April 29

JOINT MEETING

SECTION ON NEUROSURGERY

President: Irving J. Sherman, *Bridgeport*
Secretary: Franklin Robinson, *New Haven*

SECTION ON NEUROLOGY

President: James C. Fox, Jr., *Hartford*
Secretary: John C. Moench, *New Haven*

3:30 Room 408
Moderator: Francis H. O'Brien, *Waterbury*

PARKINSONISM

Clinical Manifestations of the Disorder—James C. Fox, Jr., Hartford
Correlative Neuroanatomy and Physiology—Jerome Sutin, New Haven
Medical Management—Gilbert H. Glaser, New Haven
The Role of Surgery—William B. Scoville, Hartford

SECTION ON PATHOLOGY

3:30 Room 436

President: Murray E. Rosenberg, *Willimantic*
Secretary: David J. Nelligan, *New London*

The Role of the Laboratory in the Clinical Use of Antimicrobial Agents

Louis Weinstein, *Boston; Professor of Medicine, Tufts University School of Medicine; Associate Physician-in-Chief and Chief of the Infectious Disease Service, Pratt Clinic—New England Center Hospital*

SECTION ON PHYSICAL MEDICINE

3:30 New York-Washington Rooms

Chairman: Sidney Licht, *New Haven*
Secretary: Lee B. Greene, *Bridgeport*

Rehabilitation of Spinal Cord Paralysis

William J. Erdman, II, *Philadelphia; Professor of Physical Medicine and Rehabilitation, University of Pennsylvania Medical School*

SECTION ON PREVENTIVE MEDICINE AND PUBLIC HEALTH

3:30 Room 404

Chairman: J. Wister Meigs, *New Haven*
Secretary: Ralph W. Haswell, *Hartford*

Epidemiological Studies of Coronary Disease in an Industrial Population

J. Wister Meigs, *New Haven; Associate Professor of Epidemiology (Occupational Health), Yale University School of Medicine*

Wednesday, April 29

SECTION ON UROLOGY

3:30 Room 412

President: Robert R. Berneike, *New Haven*
Secretary: James Lee Eliasoph, *Stamford*

PHYSIOLOGIC MECHANISMS IN RENOVASCULAR HYPERTENSION

HOWARD LEVITIN, *New Haven; Assistant Professor of Medicine, Yale University School of Medicine*

CONNECTICUT DIABETES ASSOCIATION

3:30 Room 440

President: Robert M. White, *New Haven*
Secretary: James C. Hart, *Hartford*

CURRENT PROBLEMS IN DIABETIC MICROANGIOPATHY

HAROLD RIFKIN, *New York; Clinical Professor of Medicine, Albert Einstein College of Medicine; Senior Attending Physician, Montefiore Hospital*

HEZEKIAH BEARDSLEY PEDIATRIC CLUB

3:30 Boston-Buffalo Rooms

President: Francis W. Helfrick, *Manchester*
Secretary: Clarence W. Harwood, *Middletown*

GLYCOGEN STORAGE DISEASES

IRA BRANDT, *New Haven; Associate Professor of Pediatrics, Yale University School of Medicine*

CONNECTICUT OCCUPATIONAL THERAPY ASSOCIATION

10:00 A.M.

Newington Hospital for Crippled Children, Newington

10:00 THE BOBATH NEUROPHYSIOLOGICAL APPROACH TO THE TREATMENT OF THE CEREBRAL PALSIED CHILD
MISS MARY FIORENTINO, *OTR, Director of Occupational Therapy, Newington Hospital for Crippled Children*

11:30 BUSINESS MEETING

1:00 LUNCHEON

3:30 The group will join the Section on Physical Medicine of the Connecticut State Medical Society at the Statler-Hilton Hotel, Hartford, in the New York-Washington Rooms

Wednesday, April 29

ANNUAL DINNER OF THE SOCIETY

Statler-Hilton Hotel
10 Ford Street
Hartford, Connecticut

Social Hour 6:15 p.m. Dinner 7:00 p.m.

PROGRAM

Introduction of Newly Elected Officers — Stevens J. Martin, *Hartford, Chairman of the Council*

Ralph L. Gilman, *Storrs, President, presiding*

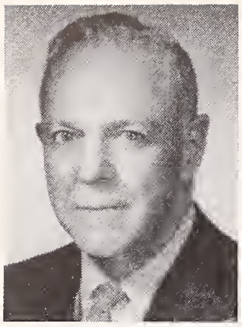
Presentation of Guests and Delegates From State Medical Societies

Fifty Year Membership Awards

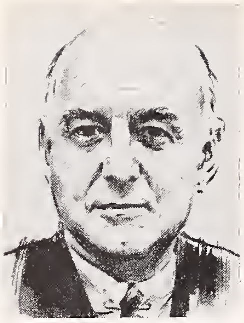
Charles William Daly, Hartford
Clinton Demas Deming, West Hartford
Edward A. Deming, West Hartford
Charles Thomas Flynn, New Haven
Edward H. Kirschbaum, Santa Barbara, California
Ralph W. Nichols, New Haven
Thomas Hubbard Russell, Mt. Dora, Florida
Raymond Harrison Ryder, Waterbury
Fred Morse Smith, Willimantic
Harold Burton Woodward, Bristol

Guest Speaker

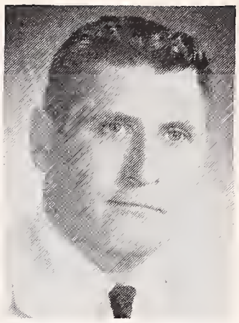
Dr. Albert E. Burke, *television commentator, lecturer and author*
Topic: "The Idiot"



Alton Ochsner
New Orleans, La.



George T. Pack
New York City



William B. Kannel
Framingham, Mass.

Leslie W. Williams
Hartford

Michael E. DeBakey
Houston, Texas

Thursday, April 30

9:00 Registration—Mezzanine

Terrace Room

Peter J. Scafarello, *Hartford, presiding*

9:45 Problems in the Treatment of Cancer

Alton Ochsner, *New Orleans; Director of Surgery, Ochsner Foundation Hospital; Emeritus Professor of Surgery, Tulane University*

10:30 Primary and Metastatic Tumors of the Liver

George T. Pack, *New York City; Attending Surgeon, Pack Medical Group; Attending Surgeon, Emeritus, Memorial Cancer Center; Associate Professor Clinical Surgery, Cornell University Medical College*

11:10 Intermission to Visit Technical Exhibits

11:40 Factors of Risk in Clinical Atherosclerotic Disease

William B. Kannel, *Framingham; Associate in Preventive Medicine, Harvard Medical College; Consultant in Medicine, Framingham Union Hospital*

(Program arranged with Connecticut Chapter-American Academy of General Practice in cooperation with the Connecticut Heart Association)

12:20 Cooperation Between Police, Medical Examiners and Doctors

Major Leslie W. Williams, *Executive Officer, Connecticut State Police Department, Hartford*

(Program arranged with Association of Medical Examiners of Connecticut)

1:00 Luncheon—City Rooms

Intermission to Visit Technical Exhibits

PROGRAM ARRANGED WITH THE CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

President: William H. Curley, Jr., *Bridgeport*
Secretary: William T. Livingston, *New Britain*
Program Chairman: James B. D. Mark, *New Haven*

2:00-3:30 General Surgical Problems—Case Presentations

Moderator: Michael E. DeBakey, *Houston, Texas; Professor and Chairman of the Department of Surgery, Baylor University School of Medicine*

Panel: Mark A. Hayes, *New Haven; Professor of Surgery, Yale University School of Medicine*

Samuel D. Kushlan, *New Haven; Associate Clinical Professor of Medicine, Yale University School of Medicine*

Arthur R. Clemett, *New Haven; Assistant Professor of Radiology, Yale University School of Medicine*

The Connecticut Society of American Board Surgeons and the Section on Radiology will have a joint social hour and dinner beginning at 5:30 in the Terrace Room.

5:30 Social Hour 7:00 Dinner

Guest Speaker: Michael E. DeBakey *Subject*: Angiography and Vascular Surgery

Thursday, April 30

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON ALLERGY

3:30 Boston-Buffalo Rooms

President: John F. Beakey, *Hartford*
Secretary: A. Arthur Fierberg, *Hartford*

Clinical Appraisal of Surgical Procedures in the Management of Chronic Bronchial Asthma

Maurice S. Segal, *Boston; Clinical Professor of Medicine, Tufts University School of Medicine; Director of Department of Inhalational Therapy and Lung Station (Tufts) Boston City Hospital*

SECTION ON ANESTHESIA

3:30 Room 424

President: John E. Keet, *Waterbury*
Secretary: James B. Given, *Hartford*
Program Chairman: Harold F. Scully, *Hartford*

3:30 Executive Committee Meeting

4:30 Business Meeting

5:00 The Use of Halogenated Hydrocarbons in Pediatric Anesthesia

Robert M. Smith, *Boston; Children's Hospital; Assistant Clinical Professor, Harvard Medical School*

EYE, EAR, NOSE AND THROAT SECTION

3:30 Rooms 436-440

President: Arthur C. Unsworth, *Hartford*
Secretary: David W. Parke, *Meriden*

The meeting will be devoted to dissolution of present EENT Section and establishment of separate Ophthalmology and Otorhinolaryngology Sections.

SECTION ON ORTHOPEDICS

3:30
Hunt Memorial Building
230 Scarborough Street, Hartford

President: Gerald S. Greene, *Hartford*
Secretary: Charles T. Flynn, Jr., *Meriden*

Scoliosis, A Second Look

William F. Donaldson, *Pittsburgh; Clinical Associate Professor, Orthopedic Surgery, University of Pittsburgh School of Medicine*

Orthopedic Complications of Hemophilia

Thomas D. Brower, *Pittsburgh; Associate Professor, Orthopedic Surgery, University of Pittsburgh School of Medicine*

Thursday, April 30

SECTION ON PROCTOLOGY

3:30 Room 404

President: Abraham Markoff, *New Haven*
Secretary: Bernard J. Kaplan, *Hartford*

Etiology and Treatment of Pilonidal Disease

Neil W. Swinton, *Boston; Department of Surgery, Lahey Clinic*

CONNECTICUT DISTRICT BRANCH – AMERICAN PSYHIATRIC ASSOCIATION

3:30 Room 408

President: George S. Hughes, *Darien*
Secretary: John H. Houck, *Hartford*
Program Chairman: Harvey R. Wasserman, *Westport*

Planning for Comprehensive Community Mental Health Services

Max P. Pepper, *New Haven; Director, Mental Health Planning Project for the State of Connecticut; Assistant Professor of Psychiatry, Yale University School of Medicine*

Discussants: Wilfred Bloomberg, Hartford
John Donnelly, Hartford
Louis B. Fierman, West Haven
George S. Hughes, Darien
Harold S. Wright, Greenwich

SECTION ON RADIOLOGY

3:30 New York-Washington Rooms

President: Wayne P. Whitcomb, *New Haven*
Secretary: Orlando F. Gabriele, *New Haven*

3:30 Business Meeting

5:30 The Section on Radiology will meet jointly with the Connecticut Society of American Board Surgeons in the Terrace Room. After-dinner speaker will be Michael E. DeBakey, *Houston, Texas, Professor and Chairman of the Department of Surgery, Baylor University College of Medicine.*

Subject: Angiography and Vascular Surgery

Thursday, April 30

ASSOCIATION OF MEDICAL EXAMINERS OF CONNECTICUT

Rooms 416-420
President: Samuel B. Rentsch, *Derby*
Secretary: Francis P. A. Williams, *Monroe*

1:00 Luncheon for Medical Examiners and Guests

3:30 Business Meeting

4:00 Discussion Concerning a Pathologist for the State Medical Examiners System

Brae Rafferty, *Willimantic, Moderator*

CONNECTICUT RHEUMATISM ASSOCIATION

3:30 Room 412
President: Harold J. Lehmus, *Manchester*
Secretary: Harold S. Barrett, *Hartford*

Population Study of Joint Disease in New Haven

Roy M. Acheson, *New Haven; Associate Professor of Epidemiology and Medicine, Yale University School of Medicine*

Business Meeting

CONNECTICUT CHAPTER OF NATIONAL ASSOCIATION OF SOCIAL WORKERS – MEDICAL SOCIAL WORK SECTION

12:15
Shoreham Oaks Restaurant
440 Asylum Street, Hartford

The Clinician Reflects on Social Work

E. Richard Weinerman, *New Haven; Director of Ambulatory Services, Grace-New Haven Community Hospital; Associate Professor of Medicine and Public Health, Yale University School of Medicine*

SPECIAL NOTES

SECTION ON OBSTETRICS AND GYNECOLOGY

Members of the Section on Obstetrics and Gynecology are invited to attend the meeting of the New England Society of Obstetrics and Gynecology at the Hotel America, Hartford, on Wednesday, April 29, 1964. Hours: 10:00 a.m. to 12:00–2:00-5:00 p.m. No separate meeting of the section will be held.

ANNUAL MEETING

CONNECTICUT MEDICAL POLITICAL ACTION COMMITTEE (COMPAC)

Thursday, April 30, 1964

1:30 – Rooms 436-440

Statler-Hilton Hotel, Hartford

Exhibitors — 1964 Annual Meeting

Space	*Firm*	*Location*
1	Group Insurers, Inc.	New Haven, Conn.
2	Merck, Sharp & Dohme	West Point, Pa.
3	Warner-Chilcott Laboratories	Morris Plains, N.J.
4	U.S. Vitamin & Pharmaceutical Corp.	New York, N.Y.
5	Arthur W. Eade Insurance Agency	New Haven, Conn.
6	Surgeon's & Physicians Supply Company	Boston, Mass.
7	Dome Chemicals, Inc.	New York, N.Y.
8	Wallace Laboratories	Cranbury, N.J.
9	G.D. Searle & Company	Chicago, Ill.
10	Mutual Benefit Life Insurance Company	Hartford, Conn.
11	Mikelk Electronics Company	Auburn, Mass.
12	Professional Equipment Company	New Haven, Conn.
13	Duke Laboratories, Inc.	So. Norwalk, Conn.
14	Wampole Laboratories	Stamford, Conn.
15	Sandoz Pharmaceuticals	Hanover, N.J.
16	Warren-Teed Pharmaceuticals, Inc.	Columbus, Ohio
17	Thermo-Fax Sales, Inc.	New Haven, Conn.
18	Lederle Laboratories	Pearl River, N.Y.
19	Conn. Chronic & Convalescent Hosp. Assoc.	Milford, Conn.
20	Carnrick Laboratories	Summit, N.J.
21	Pfizer Laboratories	New York, N.Y.
22	E.R. Squibb & Sons	New York, N.Y.
23	Syntex Laboratories, Inc.	Palo Alto, Calif.
24	Westwood Pharmaceuticals	Buffalo, N.Y.
25	Abbott Laboratories	North Chicago, Ill.
26	The Upjohn Company	Kalamazoo, Mich.
27	Brewer & Company, Inc.	Worcester, Mass.
28	Lexington Instruments Corp.	Waltham, Mass.
29	The National Drug Co.	Philadelphia, Pa.
30	Roche Laboratories	Nutley, N.J.
31	Piper Aircraft Corp.	Norwood, Mass.
32	Brookes Research Associates	Hanover, N.J.
33	Great Books of the Western World	Chicago, Ill.
34	Central Surgical Supply Co., Inc.	Ansonia, Conn.
35	Eli Lilly & Company	Indianapolis, Ind.
36	Mead Johnson Laboratories	Evansville, Ind.
37	Encyclopaedia Britannica, Inc.	Chicago, Ill.
38	Eaton Laboratories	Norwich, N.Y.
39	Lloyd Brothers, Inc.	Cincinnati, Ohio
40	Jacuzzi Research Inc.	Berkeley, Calif.
41	Ciba Pharmaceutical Co.	Summit, N.J.
42	Parke, Davis & Company	Detroit, Mich.
43	D.G. Stoughton Co.	West Hartford, Conn.
44	Ames Company, Inc.	Elkhart, Ind.
45	Organon, Inc.	West Orange, N.J.
46	Photoeaze Mfg. Co.	New York, N.Y.
47	Lessere-Wertheim, Inc.	Hartford, Conn.
48	Burroughs Wellcome & Co. (U.S.A.) Inc.	Tuckahoe, N.Y.
49	Connecticut Medical Service, Inc.	New Haven, Conn.

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YOUR KNOWLEDGE and experience in the field of medicine is appreciated by your patients who call you when they are ill and trust you to prescribe the correct treatment to cure their specific ailments.

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Reimbursements up to $10,000.00. Deductible of $500.00, $750.00, or $1,000.00. Protection after retirement, coverage for widows and children in the event of prior demise of member. All dependent children can be covered regardless of age. This same broad coverage is also available for the first time to your employees and their families.

ACCIDENT AND HEALTH PLAN

In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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William R. Richards, m.d., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1964 Annual Meeting of the House of Delegates will be held at the Statler-Hilton Hotel, Hartford, commencing at 10:00 o'clock in the morning of Tuesday, April 28.

Following luncheon, the House will reconvene for the completion of business.

Morris P. Pitock, President
Michael R. Scully, Speaker of the House
Orvan W. Hess, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENT TO THE BYLAWS

The following proposed amendment to the Bylaws was presented to the House of Delegates on December 11, 1963 and was tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, this amendment will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

INTRODUCED BY THE HARTFORD COUNTY MEDICAL ASSOCIATION

Article VII, Section 1, Paragraph 4 to be amended as follows:

"The Council shall be the Board of Censors of the Society. It shall consider all questions involving the rights and standing of members in relation to other members, to the component associations, or to this Society. In addition, all questions of an ethical nature brought before the House of Delegates or a general meeting, shall be referred to the Council without discussion. It shall hear and decide all questions of discipline affecting the conduct of members of component associations on which an appeal is taken, but only on questions of law and procedure and not on facts and its decision on all such matters will be final.

(a) The Council shall consider only the records of the component medical association in the proceedings involved.

(b) It shall determine that the record available to them is material and sufficient to support the findings which the component medical association reached.

(c) If determining that the above procedure was correct, it shall make its findings known to the appellant.

(d) If, however, finding that the procedure was not material or sufficient, it shall remand the case to the component medical association and ask for a new hearing.

(e) No appeal shall be considered or reviewed until such time as the component medical association has made its decision as to the facts in the case.

The Council shall also serve as a board of review for cases of claimed malpractice referred to it by the Committee on Medical Ethics and Deportment of any component county association."

Delegates To Annual Meeting

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, April 28, 1964, and the Semi-Annual Meeting in December, 1964, is as follows:

COUNTY	MEMBERSHIP DEC. 31,1963	OFFICIAL DELEGATES
Fairfield	907	26
Hartford	1066	31
Litchfield	142	5
Middlesex	122	4
New Haven	952	28
New London	195	6
Tolland	22	1
Windham	67	2

The Secretary's office will appreciate being informed as soon as possible, the names and addresses of all of the delegates who will represent your county at the Annual Meeting of the House of Delegates in Hartford. The Handbook for the meeting will be delivered to each delegate as soon as possible. If any of the delegates from your county association cannot attend the meeting, will you notify this office who their alternates are to be and we shall see that these alternates are supplied with the Handbook and reports.

Election Of Councilors And Associate Councilors

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Fairfield, Litchfield, New Haven and Tolland counties. In accordance with the Bylaws each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Fairfield and New Haven County Medical Associations should elect a Councilor and two Associate Councilors each for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for re-election.

Newly elected Councils and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

* * * *

At the Semi-Annual Meeting of the House of Delegates on December 4, 1962, Article VII, Section 2 of the Bylaws of the Society was amended by the addition of the following sentence after the term Councilor-at-Large:

"In the event that both the Councilor and the Associate Councilor (s) from a county association cannot be present, the President of the county association may appoint a substitute councilor."

Choosing Can Be Fun

Every so often one or another of our many excellent health insurance and prepayment agencies goes before an appropriate government commission to seek authorization to increase subscriber charges (premiums) for hospital care coverage. The two reasons most commonly advanced by the companies to justify higher rates are (a) greater hospital costs, and (b) greater hospital utilization.

One has only to read the daily newspapers to become aware that these proposals to raise rates seldom meet with public favor, to put it mildly. More often than not, a great hue and cry goes up from the politicians and the labor leaders protesting that such an increase in premium cannot be justified, that there must be some kind of hanky-panky going on somewhere, and that if the insurance companies can't manage to operate more efficiently and for less than pennies-a-day "the government will have to take over and do the job right." We have seen typical examples of this recurring protest phenomenon in the past few months, first with the Connecticut 65 Plan here in our own State, and, more recently, with the Blue Cross agencies in New Jersey and New York. "A ten per cent jump in price?," the critics scream, "Don't be ridiculous!"

But maybe our voluntary plans aren't doing so badly— at least not when we compare their performance with what appears to be happening in a place where the government *has* taken over hospital care financing. In the February 24 issue of U.S. NEWS AND WORLD REPORT, a featured article tells us that "the high and rising cost of Government hospital insurance is soon to come home to the people of Ontario, Canada's most populous Province. Effective July 1, premiums (taxes) charged individuals and families will be raised nearly 50 per cent."

The article goes on to note that the cost of the hospital program has almost doubled in the six years of its existence, and that, while the Central Government continues to pay half, it is "raising the other half (that) has been a problem in politics and finances in Ontario." It seems that for "political reasons" premium charges were frozen at the original level—although in 1961 they sneaked in a little extra 3 per cent sales tax to try to conceal the mounting deficits, but now, with hospital costs expected to go up another 14 per cent, the politicos are being forced to give the people the bad news about the "free" care they have been enjoying and to demand that they belatedly start paying the piper.

It is our judgment that, once again, the striking difference between so-called "social insurance" and bona fide private (voluntary) insurance has been clearly and convincingly demonstrated by these developments to our North. For when responsible private carriers find they must increase rates to balance their accounts, they have to come right out and say so—whether the reaction of the public proves to be favorable or not. Further, the law insists that they do this *before* their required reserves become dangerously depleted. But when "government takes over" and keeps all the books, as the Ontario story so well bears out, no such stringent procedure has to be followed. Eager officeholders see to it that the people are kept fat and happy—so they'll vote "right"—until the mounting flood of bureaucratic red ink reaches its crest and can no longer be ignored, even by the politicians themselves. Then comes the day of reckoning, and the people, if they will, can "turn the rascals out" but only at the risk of seriously jeopardizing the sole source of hospital cost protection they're allowed.

One thing we have always liked about having a variety of voluntary plans here in America is that if we figured one wasn't giving us our money's worth we could forthwith change to another. But what choice would we have if there was only one plan around—a compulsory one, like up in Ontario? And what could we do if we didn't go at all for an upcoming 50 per cent or so increase in its premium charges? A couple of times in our life we have let a few bills we didn't particularly want to pay fall conveniently behind our filing cabinet and get lost for awhile, but never once have we quite been able to get up enough courage to ignore a notice from the tax-collector's office.

W.R.R.

SUMMARY OF ACTIONS
COUNCIL MEETING

Saturday, February 15, 1964

I. Attendance

Present were: Drs. Pitock, Gilman, Hess, Weise, Sr., Scully, O'Connor, Bradley, Grendon, Grant, Davis, Phillips, Hughes, Shepard, Weber, Jr., Dean, Seigle, Gevalt, Abbot, Spitz. Also present were: Mr. Grant N. Nickerson and Dr. Richards. Absent were: Drs. Cullen, Goldberg, Gardner, Wilson, Martin, Ciccarelli, Egan, Caplan, Hastings, Major.

II. Special Business

The meeting was chaired by Morris P. Pitock, the President, in the absence of Stevens J. Martin, the Chairman of the Council. Dr. Pitock announced that he had called the meeting because he, Mr. Nickerson and Dr. Richards were in agreement that the Council should receive a report on their meeting with representatives of CMS on February 6th *in advance* of the annual meeting of CMS, Inc. which will take place on February 18th.

Following receipt of this report, the Council members reviewed and discussed almost every aspect, past and present, of the relationship between CMS and the Society, and the extent to which the original relationship has changed over the past fifteen years. Then, centering its attention on the report filed by Mr. Nickerson, Dr. Pitock, and Dr. Richards on their February 6th meeting with the CMS representatives, the Council concluded that many problems of a major and basic type presently exist between the two agencies but that, by any measure, the most disruptive problem of the moment is the uncertain and ill-defined conditions of "sponsorship" of CMS by the Society which have resulted from the changes in Article I of the CMS bylaws made by the Corporators on January 23, 1964. Dealing with this specific problem, the Council voted to adopt a resolution as follows:

WHEREAS: On January 23, 1964, Connecticut Medical Service, Inc. did, in fact, disavow the sponsorship of CMS by the Connecticut State Medical

Society by amending the CMS bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., therefore be it

RESOLVED: That, *at the regular meeting of the CSMS House of Delegates on April 28, 1964,* the Council recommend that the House recognize as a fact that, on January 23, 1964, Connecticut Medical Service, Inc. did disavow the sponsorship of the Connecticut State Medical Society by amending the CMS bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., and recommend further that the House confirm that, because of this disavowal, sponsorship of CMS by the Society no longer exists.

Thereafter, in a related action, the Council voted to adopt a second resolution as follows:

WHEREAS: Past experience has shown that no satisfactory relationship can endure between the Connecticut State Medical Society and third party agencies, such as Connecticut Medical Service, Inc., in the absence of formal legal agreements which stipulate the rights, powers, duties and obligations of each toward the other, therefore be it

RESOLVED: That the Council recommend to the CSMS House of Delegates, at its meeting on April 28, 1964, that the House establish the policy that the Society shall engage in no future sponsorship of any third party agency unless and until there shall exist formal written legal agreements between the Society and the third party agency seeking sponsorship, said agreements to specify the rights, powers, duties and obligations of the Society and of the third party concerned.

The Council then authorized its legal advisor, Mr. Nickerson, to inform his CMS counterpart, Mr. Keefe, of these actions of the Council; to reflect to Mr. Keefe the sense of the Council's deliberations at this meeting; and to advise Mr. Keefe that the Council is more than willing to pursue liaison negotiations which might develop workable solutions to the basic problems which the Council has concluded now exist between the two corporations. Further, Mr. Nickerson was asked to convey to Mr. Keefe the Council's hope that these problems might be resolved satisfactorily through liaison discussions prior to April 28, 1964, in order that it might prove unnecessary for the Council to present to the CSMS House of Delegates on that date the resolution on CMS sponsorship adopted by the Council at this February 15th meeting.

As "minimal requirements" which the Council holds must be met by the Corporators if a permanent and harmonious relationship between the two agencies is to be restored, the Council listed the following:

(1) A return to the CMS bylaws of provisions granting to the Society the right to select and name the physician Members and Directors of the Corporation, and the further right to obtain the resignation of a physician Member for stated and proven "sufficient cause."

(2) A presentation to the Society and its members of a clear and comprehensive statement of the Corporators regarding the socio-economic views and policy objectives which they propose to reflect in the immediate and future operation of CMS, Inc.; also, a definition of their concept of the meaning of "sponsorship" of CMS by the Society.

(3) A "statement of understanding" as to the conditions of sponsorship of CMS by the Society under which the CSMS House of Delegates could bestow, and the CMS Corporators would accept, such sponsorship in the future.

It should be noted that no action taken by the Council up to and including this meeting has actually affected the status of CMS, Inc. with respect to being "sponsored" by the Society, and that, at this time, no change in such status is anticipated before the annual meeting of the CSMS House of Delegates on April 28, 1964.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on February 15, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

SUMMARY OF ACTIONS
COUNCIL MEETING
Thursday, February 20, 1964

I. Attendance

Present in addition to the Chairman, Dr. Martin, were: Drs. Pitock, Goldberg, Hess, Gardner, Scully, O'Connor, Bradley, Davis, Hughes, Shepard, Dean, Seigle, Egan, Abbot, Major. Also present were: Mrs. Lindquist, Mr. Burch, Dr. Richards. Absent were: Drs. Gilman, Cullen, Weise, Sr., Wilson, Grendon, Grant, Phillips, Weber, Jr., Ciccarelli, Gevalt, Caplan, Spitz, Hastings.

II. Routine Business

Approval Of Minutes

As printed and distributed it was VOTED to approve the minutes of the meetings of January 22, 1964 and January 26, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

A. William Battista, New Haven (NHCMA)
John A. Bodie, New Haven (NHCMA)

Donald A. Bristoll, Kensington (HCMA)
George A. Gildersleeve, Norwich (NLCMA)
J. I. Kalin, Hartford (HCMA)
Marjorie Knauth, Wilton (FCMA)
Henry G. Lonsdale, No. Little Rock, Arkansas (HCMA)
Robert H. Osmond, West Hartford (HCMA)
Richard W. Pullen, Germany (HCMA)

Exemptions From Dues

It was VOTED to exempt the following members from payment of CSMS annual dues as follows:

Carter Marshall, New Haven (NHCMA)—1964
Elizabeth B. Hinckley, Guilford (NHCMA)—1964

Student Membership

It was VOTED to elect the following medical student to Student Membership in CSMS:

George J. David, 101 Mill Plain, Danbury

Resignation—Committee On Hospitals

It was VOTED to accept the resignation of Howard J. Lockward, Manchester, from membership on this Committee.

Resignation—Committee On Postgraduate Education

It was VOTED to accept the resignation of Robert J. Williamson, Bristol, from membership on this Committee.

Nominations—Hospital Advisory Committee

It was VOTED to nominate two members of the Society for appointment of one member to represent the Society on the State's Hospital Advisory Committee for a term of five years, in accordance with the General Statutes, Section 19-31.

Christie E. McLeod, Middletown
Waldo F. Martin, Milford

Appointment To Citizen's Committee For High School Driver Education

It was VOTED to request Albert L. Larson, Hartford, to act as the representative of the Society to serve on the Citizen's Committee for High School Driver Education. Dr. Larson is a member of the CSMS Committee on Accident Prevention.

National Congress On Medicine And Pharmacy

It was VOTED to direct the Chairman to select and designate two members of the Society to attend a Congress on Medicine and Pharmacy, to be held in Chicago, March 12-13, 1964 under the auspices of the Commission on Medicine and Pharmacy (made up of the AMA, the American Pharmaceutical Association and the National Association of Retail Druggists). The AMA will pay usual expenses for the attendance of two representatives of the Society.

Statewide Hospital Planning Agency

It was VOTED to accept a progress report on hospital planning filed by Leopold M. Trifari, Chairman of the Committee on Hospitals. The essence of the report was that "regional planning councils have been formed in various areas of the State (and) these . . . have been active in their own sections over the past year or so. However, a master Statewide Planning Council has not yet been formed, nor has any definite concrete activity taken place on a state level (although) it may occur soon."

Authorization—Payment Of Legal Fees

(a) It was VOTED to authorize payment to Wiggin and Dana, New Haven, of 1963 cumulative legal fees, and it was further VOTED to express appreciation to Mr. Grant N. Nickerson of Wiggin and Dana for his excellent representation of the Society in the CMS matter.

(b) It was VOTED to authorize payment to Attorney Edward L. Marcus, New Haven, cumulative legal fees for services to the Committee on Corporate Practice of Medicine.

Date Of Next Meeting

The next meeting of the Council will be held on Wednesday, March 25, 1964.

III. Old, New And Special Business

Proposal—Committee On Health Careers

Bernard F. Mann, Jr., Chairman of the Committee on Health Careers, joined the Council to report on the over-all progress of the Health Careers Program being conducted by his Committee in association with state and county Woman's Auxiliaries, and also on formal investigation he had made as to the possibility of combining this effort with those of other agencies to form a "state association on health careers" in Connecticut. Recommending that the leadership of such an association be retained by physicians, Dr. Mann requested authorization to proceed with his investigations to the point of drawing up a constitution and bylaws for such an association, determining how many voluntary health agencies in the state would wish to join, what staff personnel would be required and the financial commitment that each participating agency would be expected to make on an initial and an annual basis.

It was VOTED to express to Dr. Mann the Council's confidence in his proposal to establish a statewide association on health careers, and to authorize him to proceed with development of the plan he presented to the Council at this meeting, it being the understanding of the Council that if, in its final form the plan is acceptable to the Society, financial support by the Society is implicit, and it being understood further that no sponsorship proposal shall be made by the Council to the CSMS House of Delegates unless accomanied by *written legal agreements,* signed by the responsible officials of all other agencies involved, which outline the terms and conditions under which sponsorship by the Connecticut State Medical Society shall continue.

Report—Committee On State Legislation

As requested by the Council, Kenneth F. Brandon, Chairman of the Committee on State Legislation, filed a confidential report on the entire legislative performance of the Committee, the Society's legislative agent, and the General Manager's office during the 1961 and 1963 sessions of the Connecticut General Assembly. It was VOTED to accept Dr. Brandon's report, with thanks, and to request the Committee on State Legislation to formulate a legislative approach for the next session (1965) of the General Assembly which will more effectively coordinate the Society's staff and committee resources and provide for better utilization of the services of the Society's paid legislative agent.

Cigarette Advertising—Connecticut Medicine

After reviewing its most recent policy on accepting cigarette advertising for CONNECTICUT MEDICINE, established on October 24, 1962, it was VOTED to establish current policy on this matter by adopting a motion as follows:

IT IS MOVED: That, in keeping with the resolution on "cigarette smoking" adopted by the CSMS House of Delegates on December 11, 1963, the Council rule that advertisements of cigarettes shall *not* be accepted for CONNECTICUT MEDICINE in the future.

Resolutions—Committee On Aging

It was VOTED to adopt a series of two resolutions which had been submitted by the CSMS committee on Aging. The resolutions read as follows:

RESOLVED: That the Council of the Connecticut State Medical Society request the Governor of Connecticut to appoint a member of the CSMS Committee on Aging to membership on the Governor's Commission on Services to Elderly Persons as a representative of the Society, and be it further

RESOLVED: That the Council also request that, until such appointment is confirmed, the Governor grant official permission to a member of the CSMS Committee on Aging to attend meetings of the Commission on Services to Elderly Persons as an observer whose function will be to maintain liaison between the Commission and the Connecticut State Medical Society.

Pursuant to this action, it was VOTED to recommend to Governor Dempsey for appointment to the Commission on Services to Elderly Persons the name of Dr. George H. Gildersleeve of Norwich, Chairman of the CSMS Committee on Aging.

Connecticut Medical Service, Inc.

A comprehensive and chronological review was presented by various members of the Council covering the events which have transpired concerning CMS since the last meeting on February 15, 1964 All these reports were informal and informational and required no action by the Council.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on February 20, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

Arnaldo G. de Carvalho, age 29—M.D. Fluminense Medical School, Rio de Janeire 1958. Specialty: Internal Medicine, Cardiology, Hematology. Available July 1964.

Obstetrician-Gynecologist, age 33—M.D. State University of New York 1956. Available June 1964.

Ophthalmologist, Harvard Medical School graduate, university trained, seeks association with ophthalmologist or group. Available July 1964.

B. W. Kreel, age 30—M.D. University Saskatchewan, Canada. Specialty: Obstetrics-Gynecology. Has Connecticut license.

PLACEMENT OPPORTUNITIES

FOR SALE — Pediatric practice in New Haven County.

FOR SALE—Fully equipped office with house attached, centrally located, suburb of Bridgeport.

FOR SALE—Ten room house and office, and exclusive, going, General Practice, in South Central Connecticut—open Hosp. $35,000.

WANTED PHYSICIANS — Hartford, Middlesex, New London and Windham Counties.

FAIRFIELD COUNTY—Physician would like to share his office with General Practitioner or Internist.

PSYCHIATRIST—Association with rapid partnership or takeover of large, long-established, high-income psychiatric practice.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN.

ANNUAL COUNTY ASSOCIATION MEETINGS

New Haven, Thursday, March 19

WAVERLY INN, CHESHIRE

Business Meeting: 2:30 P.M. Dinner: 7:00 P.M.

Speaker: Dr. Alan S. Dana, United States Public Health Service, Communicable Disease Center, Atlanta, Georgia.

Subject: DOG SLED EPIDEMIOLOGY.

New London, Thursday, April 2

LIGHTHOUSE INN, NEW LONDON

Business Meeting: 6:30 P.M. Social Hour: 5:30 P.M.

Business meeting will follow dinner. Dinner: 6:00 P.M.

Hartford, Wednesday, April 8

HOTEL BOND, HARTFORD

Business Meeting: 5:00 P.M. Dinner: 7:30 P.M.

Speaker: Dr. Herman Miles Somers, A leading authority on political processes and social welfare activities. Dr. Somers is on the faculty of Princeton University.

Subject: THE PHYSICIAN AND THE COMMUNITY.

Middlesex, Thursday, April 9

SUN VALLEY RESTAURANT, MERIDEN ROAD, MERIDEN

Business Meeting: 4:30 P.M. Social Hour: 7:00 P.M.
Dinner: 7:30 P.M.

Speaker: Mr. Aubrey D. Gates, Director Field Service Division, A.M.A.

Subject: THE PATIENT YOU AND THE A.M.A.

Fairfield, Tuesday, April 14

STRATFIELD MOTOR INN, BRIDGEPORT

Business Meeting: 4:00 P.M. Social Hour: 6:00 P.M.

There will be no speaker. Dinner: 7:00 P.M.

Litchfield, Tuesday, April 14

WHITE HART INN, SALISBURY

Business Meeting: 5:30 P.M. Dinner: 7:00 P.M.

Speaker: President's address.

Subject: The Changing Image.

Windham, Thursday, April 16

VERNON STILES INN, THOMPSON

Business Meeting: 8:00 P.M. Dinner: 6:30 P.M.

Speaker and subject to be announced.

Tolland, Tuesday, April 21

OLD HOMESTEAD INN, SOMERS

Business meeting will follow dinner. Dinner: 6:30 P.M.

Speaker: William J. Watson, M.D., Esq.

Subject: AN ATTEMPT TO DEFINE AND UNDERSTAND THE PROBLEMS BETWEEN DOCTORS AND LAWYERS.

OBITUARIES

Ralph Emerson Kendall, M.D.

1895 - 1964

Dr. Ralph E. Kendall, 68, long time pathologist at the Hartford Hospital, died on January 28, at the hospital.

Dr. Kendall joined the hospital staff in 1925 and served as associate pathologist and bacteriologist. That same year he was also appointed pathologist at Manchester Memorial Hospital and, in 1930, he was appointed pathologist at Municipal Hospital, near McCook Memorial Hospital.

In 1936 he was appointed pathologist and bacteriologist at Hartford Hospital, posts he has held ever since.

He was born in Alliance, Ohio, February 21, 1895. He was educated in Mount Union College in Alliance, and Johns Hopkins University Medical School, Baltimore, Maryland. He interned at the Henry Ford Hospital, Detroit, in 1921 and 1922 and was associated with the hospital until coming to Hartford in 1925.

The foregoing record of Dr. Kendall's life bespeaks a life of generous devoted service to family, hospital, community and state. Such a record hints at, but fails to reveal fully the Wally Kendall whom his family, hospital staff, countless friends throughout the state and beyond the state's borders respected so highly, and so well loved.

For Wally Kendall was first of all a kind man, a sympathetic and warmhearted man to whom many came for advice in all manner of problems—even the last and least of the employees on his staff, for whom Wally always found time to listen to and to sympathize with, and, where possible, to advise.

His mind was fertile, always reaching out for means to improve the hospital's laboratory service, continually searching for methods whereby the profession at large could better serve the public. In his selfless and successful seeking to serve, he contributed tremendously to the reputation and 'image' for which Hartford Hospital and staff are so favorably known. His latest work, done with the cooperation of an electronics engineer, was in the development and construction of a "portable bed-scale" for continuously recording change in weight within an accuracy of 50 grams.

Despite his serious scientific traits, Wally was an extremely friendly, understanding, genial—even jovial—human being; but still a human being who battled for the right, as he saw it, vigorously and with feeling and absolute candor, but who, when the discussion threatened to become over-heated, would break the tension with a disarming smile and a humorous quip.

Wally had not been in good health for several years. The spectre of possible, prolonged, helpless invalidism hovered over him disturbingly. So, when he died abruptly in the Emergency Department of Hartford Hospital, the reaction of his family and and friends was one of shocked sadness, a sadness tempered by the full realization that Wally would have much preferred to depart the world as he did, still actively, and in full possession of his faculties, waging the battle to which his entire adult life had been dedicated—better investigation, better Medicine, better health for all.

The Department of Pathology, the Cytology at Hartford Hospital, the Blood Bank and the Cancer Society of Connecticut are in large measure his monuments; but the real, indestructible, unchanging monuments are in the hearts of the very many who so well loved this man called 'Wally.'

Hartwell G. Thompson, M.D.

John H. Dillon, M.D.

1880 - 1964

Dr. John H. Dillon died on January 27th after a brief illness.

He was born in 1880, he graduated from Yale Medical School in 1904, and interned at St. Joseph's Hospital, Providence, R.I.

Dr. Dillon served on the staff of St. Mary's Hospital, Waterbury, Connecticut from the year it was founded (1908) until he retired in 1963.

In 1960 Dr. Dillon was honored by the Connecticut State Medical Society when he was awarded a special certificate in recognition of half a century of service in the medical profession.

He was also past president of the Waterbury Medical Society.

After his retirement, he made his home at Longwood Towers, Brookline, Massachusetts where he died at the age of 83.

Apart from his great, lifelong love of medicine, he was an enthusiastic golfer for many years at the Watertown Golf Club.

His son, John A. Dillon, is also a member of the profession, practicing in Providence, R.I.

The many friends he made during his long professional life mark with sorrow the passing of a fine, sincere practitioner of the art.

Joseph F. Burke, M.D.

Donald A. Bristoll, M.D.
1898 - 1964

Dr. Donald A. Bristoll died at the age of 65 on February 21, 1964, at his home of leukemia. He served as chief of Obstetrics and Gynecology at the New Britain General Hospital for eighteen years until mandatory retirement this year. He established the residency training program and was widely recognized for his activities in this field. His service was one of the finest, with an enviable infant and maternal mortality rate. He was one of the founders of the Grove Hill Clinic.

In 1960 he received the American Cancer Society Bronze Medal and citation from the Connecticut division for distinguished service as past president and longtime member of the Society.

Dr. Bristoll was a diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American Medical Association and a member of the American College of Obstetrics and Gynecology, the Connecticut State Medical Society and the Hartford County Medical Association. His loss to the City of New Britian and to the New Britain General Hospital was great.

Bliss B. Clark, M.D.

In Memoriam

Cobey, James F. — New Haven; Yale Medical School, 1916. Dr. Cobey was an eye, ear, nose and throat specialist in the New Haven area for more than 40 years. He served with the U.S. Army Medical Corps as captain for one year. Dr. Cobey was a member of the staff of the Yale University Department of Health. From 1953 to 1954 he served as chairman of the Eye, Ear, Nose and Throat Section of the Connecticut State Medical Society. Dr Cobey was a member of the American Medical Association, the Connectciut State Medical Society, and the New Haven County Medical Association. He was a diplomate of the American Board of Ophthalmology and Otolaryngology, and a Fellow of the American Academy of Ophthalmology and Otolaryngology. Dr. Cobey died February 23, at the age of 71.

Paladino, Joseph S.—Hartford; Boston University Medical School, 1926. Dr. Paladino practiced medicine in Hartford for 38 years prior to his retirement. He was associated with the staff of the Hartford Hospital. Dr. Paladino was a member of the American Medical Association, the Hartford County Medical Assocation, and the Connecticut State Medical Society. Dr. Paladino died February 12 in Clearwater, Florida, at the age of 66.

Robertson, Gordon F.—Greenwich; College of Physicians and Surgeons of Columbia University, 1941. In 1941 Dr. Robertson entered the U.S. Navy, and served with the amphibious force, First Beach Battalion. He was discharged in 1947 with the rank of lieutenant commander. Dr. Robertson was a member of the American Medical Association, the Connecticut State Medical Society, the Fairfield County Medical Association, and the Greenwich Medical Society. He was a member of the board of directors of the Connecticut Heart Association; board of trustees of the Fairfield County Medical Association and the Greenwich Medical Society; board member of the Community Chest and

Council; and he served on the Home Service Committee of the American Red Cross. Dr. Robertson died February 6, at the age of 49.

Simmel, Else R.—Norwich; University of Heidelberg, 1918. Dr. Simmel was affiliated with the State Sanatorium, Uncas-on-Thames. She was a Fellow of the American Medical Association, the Connecticut State Medical Society, the Norwich Medical Society, the New London County Medical Society, and the New York State Medical Society. Dr. Simmel died February 15, at the age of 69.

Sullivan, Daniel—Quaker Hill; New York University, 1897. Dr. Sullivan was associated with the Joseph Lawrence Free Public Hospital in 1912 as staff surgeon and was soon made senior staff surgeon. In 1929 he was appointed chief of staff. In 1934, having reached the age of 60 years, he was tranferred to the consultant staff in accordance with a regulation he himself had been instrumental in passing. During World War II, Dr. Sullivan worked with a committee of Connecticut physicians, following a plan advocated by the surgeon general of the Army, to direct activities in medicine and medical care as part of the national preparedness program. In 1941, Dr. Sullivan was appointed by the then Mayor Robert B. Chappell to organize the New London Civilian Defense program and in 1942 resigned from this post. However, during the time he headed the council, he set up an organization of 30 subcommittees with a backlog of 3,000 volunteer workers. In 1942 he was elected chairman of the emergency medical services of the city in the civilian protection divsion of the Civilian Defense Council. Dr. Sullivan was a member of the American Medical Association, the Connecticut State Medical Society, and the New London Medical Association, and a Fellow of the American College of Physicians and Surgeons. Dr. Sullivan died February 19, at the age of 89.

Notice Concerning Cough Medicine And Paregoric

Because of widespread abuses in the purchase and use of cough syrups and other medication containing codeine or opium, the 1963 General Assembly by Public Act 338 (Section 19-263a of the General Statutes) authorized the State Department of Health to prohibit over-the-counter sales of certain narcotic preparations that possess a degree of addiction liability and are abused by some of those who purchase them.

Regulation 19-263-1 to accomplish this purpose was approved by the State Public Health Council on September 12, 1963, was published in CONNECTICUT MEDICINE, page 789, in December, 1963, and will take effect April 15, 1964. After that date camphorated tincture of opium, commonly known as paregoric, without a medical prescription will be available only in half ounce quantities each 48 hours and cough syrup containing codeine cannot be sold without medical prescription.

In recent years there has been increasing evidence that heroine addicts use cough syrups containing codeine to supplement their addiction. Many other instances have come to light of young people being introduced to more serious addiction by means of codeine-containing cough syrup as well as other legend drugs. In the Hartford area a study covering the period from October 1, 1961 through January 10, 1962, revealed that approximately 350 persons violated the narcotic laws by the use of false names and addresses or by purchasing excessive amounts of these narcotic drugs. Of this number, 125 persons who were previously known narcotic violators were found to have four or more illegal purchases of cough syrups.

A question has been raised whether the State Department of Health might deprive people, not sick enough to need to see a physician, of a drug necessary to relieve an unpleasant cough because of this new requirement of a medical prescription to obtain cough medicine with codeine.

In response to this inquiry it might be pointed out that there are several non-addictive drugs of low toxicity which are equivalent in value to codeine in reducing or eliminating the cough reflex. Among these are carbetamine citrate which is sold under at least four brand names, noscapine hydrochloride with six brand names, and dextromethorphan hydrobromide sold under at least 17 brand names. Since medication of this potency is readily available without prescription, it is expected that those persons whose cough persist will benefit by a thorough medical check-up. If physicians find instances where undue suffering occurs by the requirement that a medical prescription be obtained for cough syrups containing codeine, the State Department of Health will appreciate being informed of the particulars of such situations.

WOMAN'S AUXILIARY

President
Mrs. Fritz Meyer, Bridgeport

President-Elect
Mrs. Charles M. Krinsky, New London

First Vice-President
Mrs. James F. Jones, Danielson

Second Vice-President
Mrs. Ralph T. Tella, Stamford

Recording Secretary
Mrs. M. Walter Radowieki, Hamden

Corresponding Secretary
Mrs. Nicholas Creaturo, Trumbull

Treasurer
Mrs. Edwin R. Connors, Hartford

Annual Meeting April 29th

The annual meeting of the Woman's Auxiliary to the Connecticut State Medical Society will be held at Tumblebrook Country Club, 17 Simsbury Road, Bloomfield on April 29, 1964. This will be a luncheon meeting. The guest speaker William B. Walsh, M.D., President of People to People Health Foundation will speak on "Project HOPE." Dr. Walsh will be remembered as one of the featured speakers at the National Auxiliary Convention.

The business session will be held in the morning prior to the luncheon and will include annual reports and the election of officers for 1964-1965. Members are urged to make early reservations for this important meeting. Further details will be sent to the membership.

Legislative Committee

Mrs. William R. Richards and Mrs. Irving Krall, co-chairmen. This committee has been busy reading missives from A.M.A. President Dr. Annis, A.M.A. Auxiliary President, Mrs. Stoltz, and A.M.A. Auxiliary Legislative Chairman, Mrs. Leonard, passing this information on to County Chairmen, and sending letters to Washington—all about the Medicare Bill—The Hospital Insurance Act of 1963 (H.R. 3920). Also, we have attended a hearing in Hartford and a meeting on fluoridation.

The House and Ways Committee of the House of Representatives has concluded its hearings on H.R. 3920. They are expected to soon vote on whether to release it to the House. We urge that all Auxiliary members watch the paper for this event. When it is released we urge that you start a letter writing campaign to your representative and the two senators from the state. Also keep in touch with your local medical society Operation Hometown Committee and offer your assistance as needed.

These are the immediate needs on legislation. The overall need is for every Auxiliary member to show interest in being informed and being active in the political picture. The all-important national elections are coming up. Be sure you are registered, be sure to vote, become acquainted with the workings of local political groups, let your wishes be known by attending political meetings, asking questions, helping with the mechanics of nomination and election. These are the privileges and duties of all citizens including doctors and their families.

Notes

The film "Gift of Health" was shown to the state Board members at the January meeting. This film, presented by the Legislation committee is recommended for use by the counties, where possible, as a means of educating people to the issues involved in King-Anderson legislation and the reasons for opposing it.

Hartford County held the annual Medi-Capers dance in January to augment the scholarship fund. Ten medical students are receiving aid from this fund this year.

New Haven county voted recently to give its annual scholarship in memory of the deceased members of the Auxiliary of the preceding year.

Fairfield County realized over $1,000. on a raffle of leather and gift items.

Advertising Appreciated

Advertising is part of the American way of life and essential component in the competitive free enterprise system. We often take it for granted and perhaps need to be reminded of its importance to us. The participation by advertisers makes CONNECTICUT MEDICINE possible. Use the advertisers index and where appropriate, mention to the detail man that you saw his company's participation in CONNECTICUT MEDICINE.

We wish to thank each CONNECTICUT MEDICINE advertiser for his continued support for 1964.

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dependable: 'Miltown' (meprobamate) is an established drug. There are no surprises in store for you or your patient. You can depend on it to help your patients through periods of emotional distress — and to help maintain their emotional stability.

easy to use: Because 'Miltown' (meprobamate) is compatible with almost any other kind of drug therapy, you'll find it fits in easily with any program of treatment you are now using. It will not, therefore, complicate treatment of patients seen in clinical practice.

Side effects: Slight drowsiness may occur and, rarely, allergic or idiosyncratic reactions, generally developing after 1 to 4 doses of the drug.

Contraindications: Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: Should administration of meprobamate cause drowsiness or visual disturbances, the dose should be reduced. Operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Prescribe cautiously and in small quantities to patients with suicidal tendencies. Massive overdosage may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after prolonged use at high dosage. *Complete product information available in the product package, and to physicians upon request.*

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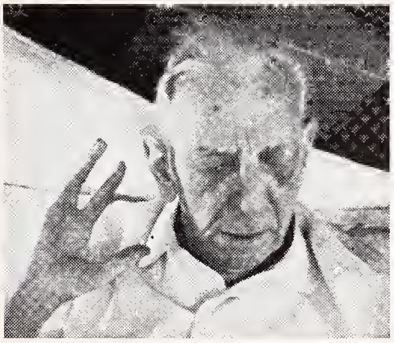

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Doctor's Office

Angelo L. Gentile, M.D. announces the removal of his office from 291 Whitney Avenue to 1488 Chapel Street, New Haven.

Sami E. Kassim, M.D. announces the opening of an office for the practice of pediatrics, in the Professional Building off White Plains Road, Trumbull Center.

Pediatric Associates of New Haven announces the opening of offices for the practice of pediatrics and pediatric allergy at Doctors Building, 2 Church Street South, New Haven. The following doctors are associated: Morris Y. Krosnick, M.D., Sidney Hurwitz, M.D., Paul Goldstein, M.D., William E. Lattanzi, M.D. and Leonard S. Krassner, M.D.

Around The State

New Haven

Dr. John S. Millis, president of Western Reserve University, will be the guest lecturer at the ninth annual D. Spencer Berger Lecture, sponsored by the Board of Directors of Grace-New Haven Community Hospital. The lecture will be held at 5:00 p.m., Thursday, April 30, 1964, in the Mary S. Harkness Auditorium of the Yale University School of Medicine.

Dr. Millis currently is chairman of the Citizens Commission on Graduate Medical Education of the American Medical Association, and has served as a director and vice president of the National League for Nursing.

Physicians, hospital trustees and administrators are invited to attend the lecture.

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CLINICAL ASPECTS OF DIAPULSE THERAPY AS AN ADJUNCT IN GENERAL OFFICE PRACTICE

WEDNESDAY, APRIL 22, 1964

ST. VINCENT'S HOSPITAL AUDITORIUM

2820 Main St., Bridgeport, Conn.

Promptly at

11:30 A.M.—Luncheon—3:00 P.M.

Papers on clinical efficacy of Diapulse electromagnetic energy in daily office use will be presented by:—

Chairman:

William D. Pasquariello, M.D.,	Bridgeport Conn.
Wilbur H. Caney, M.D.	Watertown, Conn.
Howard M. Sapiro, M.D.	Portland, Maine
Robert A. Friberg, M. D.	Arlington, Mass.
Chaim J. Wildman, M.D.	Pittsfield, Mass.
Frank D. Riccio, M.D.	Stratford, Conn.
George H. Hurwitz, M.D.	Hartford, Conn.
Arthur F. Sullivan, M.D.	Waterbury, Conn.

There will be Panel Discussions and an Open Forum

Please forward symposium attendance acknowledgements to

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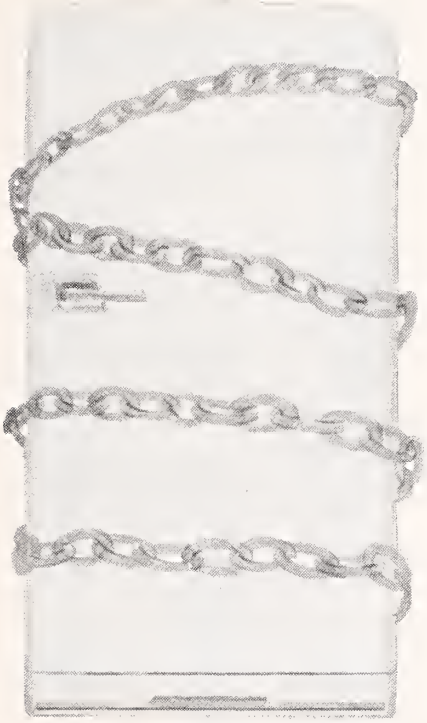

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In obesity, “...our drug of choice has been methedrine (methamphetamine hydrochloride)...because it produces the same central effect with about one-half the dose required with plain amphetamine, because the effect is more prolonged, and because undesirable peripheral effects are significantly minimized or entirely absent.” Douglas, H. S.: West. J. Surg. **59**:238 (May) 1951.

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Special Notices

MANCHESTER MEMORIAL HOSPITAL NOON CONFERENCES

Wednesday, April 8—"Recognition of Common Skin Disorders"
Dr. Myles Standish

Wednesday, April 15—"Treatment of Skin Disorders: Pruritis"
Dr. Myles Standish

Tuesday, April 21—"Hyperparathyroidism"
Dr. Ralph Reinfrank

Tuesday, April 28—"Drowning"
Dr. Donald Egan

Tuesday, May 12—Topic to be announced
Dr. Louis Weinstein

Tuesday, May 26—"Management of Acute Abdominal Trauma"
Dr. Ira S. Goldenberg

Friday, May 29—"Physical Conditioning for the Prevention of Athletic Injuries"
Dr. Allan J. Ryan

HARTFORD HOSPITAL SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS

May 1 to June 18, 1964

May 1-2—Visiting Ob-Gyn

Albert H. Aldridge, M.D., Chief Department of Ob-Gyn, The Woman's Hospital, New York City
Subjects: 10:00 a.m. "Stress Incontinence"
11:00 a.m. "Bilateral Oophorectomy at the Time of Hysterectomy"

May 8-9—Visiting Internist

Henry G. Kunkel, M.D., Rockefeller Institute, N.Y.C.
Subject: "Abnormal Proteins and Abnormal Reactions"

May 16

Research Symposium on "Aging"
Doctors E. Howes, William Wawro, Howard Wetstone and Rudolph LaMotta

May 21-23—Visiting Surgeon

William Altmeier, M.D., Prof. of Surgery, Univ. of Cincinnati
Subjects: 10:00 a.m. "The Incidence of Wound Infections on an Active Surgical Service"
11:00 a.m. "The Role of Antibiotics in Surgical Practice"

May 30

Holiday—No Clinic

June 6

John K. Lattimer, M.D., Director, Squier Urology Clinic Columbia-Presbyterian Medical Center, N.Y.C.
Subject: 11:00 a.m. "Renal Tuberculosis"

June 18

H.H. House Staff Graduation—Alumni Reunion

THE 6TH WORLD MEDICAL ASSEMBLY IN ISRAEL

August 2-14, 1964

The American Physicians Fellowship, an organization of 3100 physicians who are non-resident fellows of the Israel Medical Association, announces that the Israel Medical Association will conduct its 6th World Assembly in Haifa, Jerusalem and Tel-Aviv, Israel from August 2 to August 14, 1964.

Many world famous physicians are scheduled to lecture at this Assembly. Some of the expected speakers are Drs. Albert B. Sabin, Cincinnati, Ohio; Joseph L. Melnick, Houston, Texas; Matilda Benyesh-Melnick, Houston, Texas; Robert J. Huebner, Bethesda, Maryland; George Barski, Villejuif (Seine), France; J. Berenblum, Rehovoth, Israel; A. Kohn, Ness Ziona, Israel; N. Trainin, Rehovoth, Israel; L. Sachs, Rehovoth, Israel; N. Goldblum, Jerusalem, Israel; A. Hochman, Jerusalem, Israel; Maurice Tubiana, Villejuif (Seine), France; F. Baclesse, Paris, France; Charles Huggins, Chicago, Illinois; David A. Karnofsky; New York, New York; E. Ratzkowski, Jerusalem, Israel; Milton Friedman, New York, New York; H. Ungar, Jerusalem, Israel; E. Robinson, Jerusalem, Israel.

The American Physicians Fellowship is conducting a 24 day jet flight tour to Israel and three European capitals in conjunction with the 6th Word Assembly. Information and details about the Assembly or tour can be obtained by writing to the American Physicians Fellowship at 1622 Beacon Street, Brookline, Massachusetts 02146.

AMERICAN ACADEMY OF PHYSICAL MEDICINE AND REHABILITATION

August 24-27, 1964

The Annual Meeting of the American Academy of Physical Medicine and Rehabilitation will be held on August 24-27, 1964, at the Statler-Hilton Hotel, in Boston, Massachusetts. It will consist of formal lectures, as well as educational seminars in the field of Disability Evaluation, Forensic Physiatry, and Muscle Diseases.

Connecticut Heart Association

The Connecticut Heart Association will hold its Annual Meeting and Scientific Session for physicians and laymen May 20, at the Hillandale Country Club, Daniels Farm Road, Trumbull.

Three outstanding physicians in the field of cardiovascular disease will hold a panel discussion on "Are Heart Attacks Preventable?"

Participating will be Dr. Jeremiah Stamler Director, Heart Disease Control Division, Chicago Board of Health; Dr. George Christakis, Medical Director, Bureau of Nutrition, New York City Health Department; and Dr. David Gelfand, Chairman, Heart Association Rehabilitation Committee.

Reservations and programs will be available from your local Heart Association Chapter or the Connecticut Heart Association, 65 Wethersfield Avenue, Hartford.

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BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

A Savage Place. By Frank G. Slaughter, Doubleday & Company, Inc., Garden City, New York, 1964, 248 pp. $4.50.

Appraisal Of Current Concepts In Anesthesiology. Edited and assembled by John Adriani, M.D., Volume 2, The C. V. Mosby Company, St. Louis, 1964, 468 pp. $10.75.

Pediatric Therapy. By Harry C. Shirkey, with seventy-two contributors, The C. V. Mosby Company, St. Louis, 1964, 1052 pp. $16.50.

Heredity And Human Life. By Hampton L. Carson, Columbia University Press, New York and London, 1963, 214 pp. $5.00.

The Origin Of Adaptations. By Verne Grant, Columbia University Press, New York and London, 1963, $12.50.

1964 MEETINGS

April 28-30—Annual Meeting Connecticut State Medical Society, to be held at Statler-Hilton Hotel, Hartford.

May 13—American Academy of Pediatrics, Connecticut Chapter, to be held at Culinary Institute, 393 Prospect Street, New Haven, at 7:00 P.M. Speaker: Dr. Robert Kugel, Prof. of Medical Sciences, Brown University, Providence, R.I.

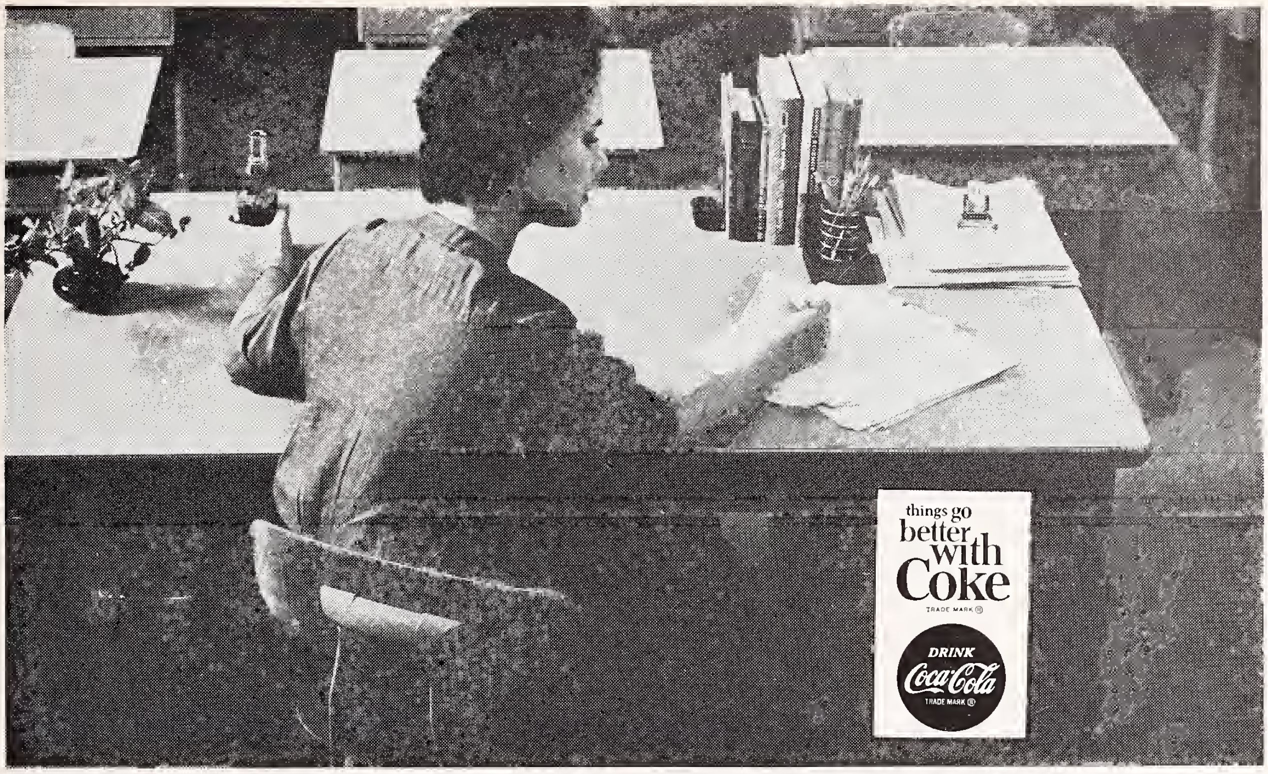
May 20—Annual Meeting Connecticut Heart Association to be held at Hillandale Country Club, Trumbull.

May 25-27—Annual Meeting American Thoracic Society Medical Section of the National Tuberculosis Association to be held in New York City.

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.



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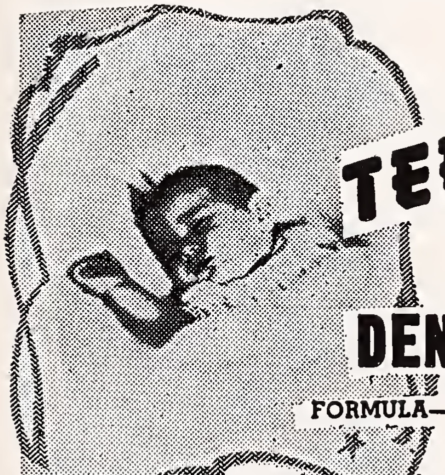

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BOOK REVIEWS

THROMBOPHLEBITIS by Roger M. Morrell, M.D., Grune & Stratton, New York and London, 1963, 182 pp. $6.50.

Reviewed by: LOUIS H. NAHUM

In this excellent book thrombophlebitis is the starting point of a historical, clinical and experimental review of the whole area of venous disease. The extent of the literature reviewed, almost 1,000 references, suggests the scope of the author's study and thought. The details of the differentiation between thrombosis, thrombophlebitis and phlebothrombosis are brought out in various of the sections.

It seems that with all we know about clotting and clotting factors no one has yet taken a thrombophlebic clot to determine the amount of mechanical strain necessary to produce friability. No one has replaced such a clot within a model vessel and reproduced the parameters of flow encountered by the clot in vivo. Raising such problems gives us a glimpse of the authors search first for what is unknown, uncommon and unexpected in this area and second, for clues as to the cause of this commonest fatal disease from well documented and unusual phenomena.

One fact emerges from his review and that is that most often thrombophlebitis does not behave in a classical fashion and that there is no way of predicting whether a patient will have a venous thrombosis, although he is more likely to have one if he has suffered with one previously.

His views on prevention, by early ambulation, anticoagulation, deep breathing exercises and avoiding tight abdominal dressings are generally accepted. His views of passive and active exercises of the legs and elevation of the foot of the bed in patients who must remain quiet are standard. His rejection of elastic stockings is not generally accepted or followed. In short, there will not be complete agreement with all his views nor is such a position desirable.

Areas previously neglected are spot lighted here such as nervous and hormonal influences, tumor metabolites and tissue factors. Also new ideas on pathogenesis and further investigations have been introduced, such as counter current and auto-immune theory of venous disease, mathematical tools for dealing with coagulation and thrombosis, electrical analog methods, information theory, and control system theory.

When one has finished the book, however, the initial three pronged concept of Virchow—local changes in blood vessels—stasis—alterations in coagulability of the blood, remain as a basic theoretical tool although each of its three parts continue to assume new dimensions.

In the last twenty-five years investigations in the field of venous disease has been accelerated from two major directions. One is the use of anticoagulants which has required more precise evaluations of the diagnosis and treatment of these syndromes. The other is the experimental studies with thrombolytic agents which have added new impetus even though these substances are not yet ready for general use. It is therefore, an appropriate time for someone to review the present state of our knowledge and our ignorance and to suggest new directions for attack. Roger Morrell has done both exceedingly well.

TIME, CELLS, AND AGING by Bernard L. Strehler, Gerontology Branch, Baltimore City Hospitals, Baltimore, Maryland, Academic Press, New York and London, 1962, 270 pp. $2.95.

Reviewed by: LOUIS H. NAHUM

The present monograph is an attempt to summarize the major lines of information on aging. In doing this the author indicates some of the major areas for theoretical and experimental exploration. Although there is as yet, not present an acceptable theory of aging, much information is brought out about the adverse changes in living systems which as a result of evolutionary inadequacies lead to abnormal chemical activities in different enzyme systems and in intercellular deposits.

In reading this book one sees at once that aging is characterized by a gradual deterioration of structure and function. Organisms die because they are unable to overcome the challenges to their continued existence. This will depend upon the absolute magnitude of the challenge as well as the magnitude of the resources available to the organism to offset the disruptive effects of the challenge. What happens to various organs, tissues, cells and subcellar components are discussed in detail. As damaged cells die, they are discarded, but this would mean a gradual loss in those tissues that cannot regenerate like the brain, muscle heart etc. Thus these organs gradually decline and become increasingly vulnerable to challenges.

This book is fascinating reading for all interested in the aging process as well as students of biochemistry, cell physiology, embryology and medicine. The amount of knowledge needed is so great and the urgency for understanding the aging process so compelling that at the end the author makes an eloquent plea for a more organized approach in this area of research.

THE CARE OF THE GERIATRIC PATIENT, 2nd Edition, Edited by C. V. Cowdry, Ph.D., The C. V. Mosby Company, St. Louis, Missouri, 1963, 566 pp. $11.85.

Reviewed by: IRA S. GOLDENBERG

The practice of medicine in the elderly patient is rapidly becoming a specialty in itself and the first edition of the present volume was most welcome in 1958. The second edition has been enlarged somewhat, but most important, places emphasis on the clinical aspects of care of the aged patient rather than on the aging process itself. Dr. Cowdry has assembled a group of experts who have contributed chapters on such diverse aspects of geriatric medical practice as dental, sexual, home care, nutritional and even selection of a nursing home as well as the more commonly recognized specialty areas of general surgery, urology, orthopedics and cardiovascular problems. The authors write with conviction from their vast experience in these areas and perform in this volume a commendable service to all practitioners.

Portions of material presented in this volume can be found in several periodicals, but never has so much valuable information on the medical problem of the aged been made so easily available. This volume is an excellent source book for all physicians who number aged persons among their patients and it is highly recommended reading for generalists as well as specialists. It is unfortunate that the price of this volume is so high since it is certain that it would have a much greater circulation were it more reasonably priced.

THE STORY OF BLOOD by Kenneth Walker, M.A., M.B., B. Ch., F.R.C.S., F.I.C.S., Philosophical Library, Inc., New York City, New York, 1963, 213 pp. $6.00.

Reviewed by: DAVID M. LITTLE, Jr.

Medicine has been associated with magic in the public mind since the days of the first witch doctors. Within the past few decades, however, a whole school of medical writers, whose prototypes were Paul de Kruif, Logan Clendening, and Howard Haggard, has appeared to explain medicine to the public and dispel its mysteries. Lay magazines such as *Reader's Digest, Good Housekeeping, Life, Time, McCall's,* the *Saturday Evening Post,* and even the *New Yorker,* regularly expound on disease processes, describe the details of the most intricate surgical procedures, explain the advantages and disadvantages of the newest drugs, and advise the reader on the preferred mode of treatment for a specific pathological condition often before the reader's physician has had access to the facts concerning the therapy in the medical journals. Occasionally, when public interest promises to be sufficient to warrant it, the prolific medical writer will expand beyond a mere article or two and produce an entire volume on a popular medical subject.

The Story of Blood is just such a book. It begins with a quotation by Mephistopheles in *Faust,* "Blood is a juice of the rarest quality," and then runs the gamut of almost all of the medical aspects of blood up to and including the use of heart-lung machines for open-heart surgery. In the course of things, it covers the development of the vascular system, the composition and functions of blood, the anatomy and physiology of the heart and its control, the significance and nature of blood pressure, the diseases of the blood, the history of blood transfusion and its uses, the immunological and anti-bacterial defenses provided by blood, blood poisoning, malaria, and even the effects of radiation. Throughout the whole, there are constant references to medical history and frequent explanations of classic medical or scientific observations and experimentations.

The book is written in a narrative style that is semi-historical and semi-philosophical, with frequent excursions into straight-forward descriptions of anatomy, physiology, pharm-

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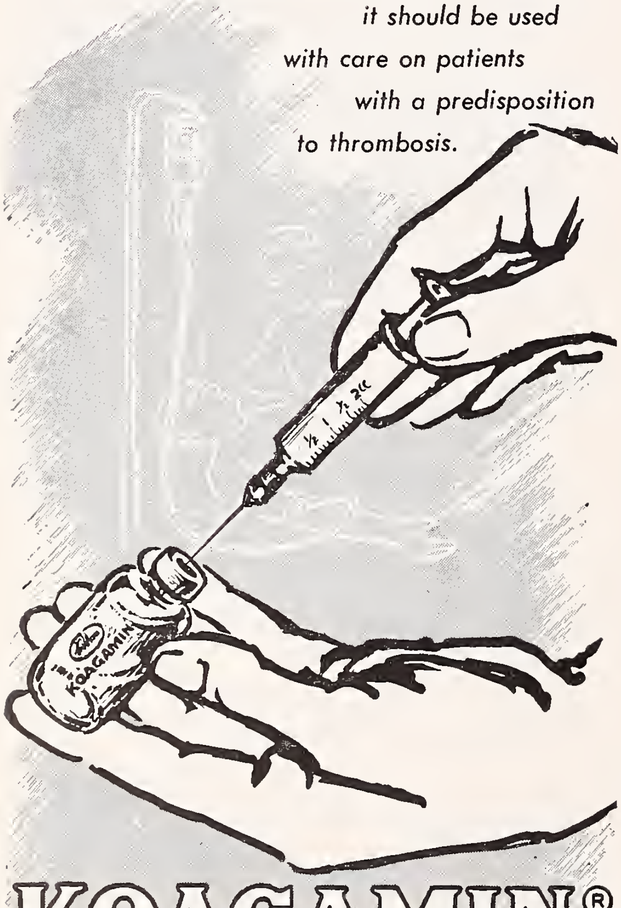

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acology, pathology and the like, in language chosen for lay comprehension. It is a volume that most practising physicians will not be able to afford the time to read for the sake of the history and philosophy that it contains, but one that should satisfy the hunger of the school or college student who yearns for the romance of medicine and things medical.

PEDIATRIC CARDIOLOGY by Alexander S. Nadas, M.D., Second Edition, W. B. Saunders Co., Philadelphia, Pennsylvania, 1963, 828 pp. $16.00.

Reviewed by: LOUIS H. NAHUM

This second edition is larger than the first and almost every page has been changed, reflecting the rapid expansion of knowledge in this field in only seven years. In fact the author expresses his chagrin over the need for revision of the "revision" even before it reached the publishers.

Like the first edition, the book consists of three parts. Part I is called the Tools of Diagnosis. It considers history, physical examination and routine tests, radiology of the heart, electrocardiography, vectorial approach, phonocardiography and cardiac catheterization. Part II is devoted to acquired heart disease and Part III to congenital heart disease. There are many more references in the bibliography than in the first edition. An appendix containing all tabular data and an extended index complete the book.

The structure of the book shows what has happened to pediatric cardiology in the last twenty-five years, for the bulk of this book is devoted to diagnosis and treatment of congenital malformations. Before Gross in 1939 showed that it was possible to correct deformities in the heart, pediatric text books devoted few pages to heart diseases in children for there was no cardiac catheterization, no useful roentgen ray diagnosis and no open heart surgery. Congenital heart disease was discussed in a few pages as a subject not meriting much space, because of the helpless and hopeless prognosis. This is all changed. With hope that something can be done interest in diagnosis came suddenly to life.

The author is well qualified for his task. He served a pediatric residency at Children's Hospital in Boston, practiced pediatrics for four years in a small town and returned to the Children's Hospital where he is now cardiologist. He is termed "a thoughtful and resourceful doctor of infants and children, a wise specialist of large experience in cardiology, a teacher of great skill and enthusiasm." This encomium is certainly deserved as becomes clear as one goes through this scholarly and thorough coverage in these pages. Only first hand information is discussed by the author who has obviously had a wealth of experience in his chosen field.

This book is for every pediatrician who should not allow all aspects of diagnosis and treatment to be handed over to a new subspecialty in cardiology. The nonsurgical aspects of cardiac disease in infancy and childhood should remain pediatric responsibility. To meet the new and growing challenge the pediatrician will find this volume extremely helpful, for it comes out of a vast personal experience of the author. Not alone for the pediatrician but also for the internist and cardiac surgeon will this book serve an important function. It is recommended highly as a scholarly work by a scientist and practicing pediatrician.

Connecticut Medicine

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Medical Journal

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THE CODE OF HAMMURABI (see page 325)

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editorials

Science Tools:

7. The Ophthalmodynamometer

When arterial pressures are measured in both arms a significant difference between them is strong evidence of a stenosis of the subclavian artery on the side with reduced pressure. If it were possible to measure the ophthalmic artery pressures in each eye it should similarly reflect stenosis or occlusion of the internal carotid artery of which the ophthalmic artery is a branch. It has been estimated that more than 20 per cent of infarctions of the cerebral hemispheres are caused by lesions of the internal carotid artery and therefore knowledge of opthalmic artery pressures should throw light upon the presence or absence of stenosis in this important vessel.[1,2,3]

The ophthalmodynamometer has been fashioned to record the measurement of ophthalmic artery pressures. It consists of a cup attached by a lever to a spring which records pressures in grams. The cup is applied to the globe over the upper lid. In the past, application of the foot of the pressure gauge to the sclera of the eye and simultaneous use of the ophthalmoscope to visualize disappearance of flow through the retinal artery, has been cumbersome and led to resistance to use of the instrument, first because of fear of the possibility of injury to the globe and second because of lack of skill in the use of the ophthalmoscope. It therefore became desirable to develop a method of circumventing the necessity of an ophthalmoscopic examination as well as avoiding the risk of traumatizing the globe.

The drawbacks have now been circumvented by Toole[1] who suggests a quick easy and safe method for determining the relative arterial pressures in the two eyes. Instead of the customary method of using the ophthalmoscope to visualize the central retinal artery, Toole has the patient cover one eye and fix his gaze on a distant object with the other. The gauge is applied to the upper lid (not the sclera) of the uncovered eye and the patient is asked to report the moment he perceives diminution of peripheral vision (gray-out) and then the instant when total loss of vision (black-out) occurs. The pressure is slowly applied to the globe through the lid until the patient indicates loss of peripheral vision, at which time the ophthalmodynamometer is read. This represents the diastolic pressure of the ophthalmic artery. Pressure is then increased until the patient reports complete loss of vision which occurs at systolic pressure of the ophthalmic artery and the gauge is read again. The same procedure is repeated on the other eye.

At this point no absolute standards have been established. Nevertheless, a difference of more than 15 per cent of the systolic or 20 per cent in the diastolic pressure on the two sides is considered suspicious of unilateral carotid artery disease. If the retinal pressures recorded in grams on the ophthalmodynamometer are equal in each eye but are less than half the brachial artery pressure recorded in mm. Hg., then there is reason to be suspicious of disease in both internal carotid arteries. Such a finding justifies the pursuit of more precise studies.[4]

We owe to Duane *et al*[5] the method of circumventing the ophthalmoscopic examination. They ascertained that peripheral vision is lost at the diastolic pressure of the ophthalmic artery whereas central vision fades at the systolic level. In a reliable patient who is able to report accurately the loss of vision which he perceives, there is therefore no need to visualize the retinal vessels while compressing the globe. This coupled with the fact that the globe cannot be traumatized when the pressure is applied over the lid, removes the obstacle to the use of ophthalmodynamometer in the physicians office.

L.H.N.

THE COVER

THE CODE OF HAMMURABI

THE clay tablets of ancient Mesopotamia document the practice of medicine as early as 3000 B.C. Of significance to medicine, too, is one of the oldest regulatory laws, the Code of Hammurabi, promulgated by that Babylonian ruler about 2000 B.C. In a Babylonian throne room, a physician is defending with dignity his professional practices against the complaints of a dissatisfied patient who seeks invocation of the drastic penalties of the Code. The King, the scribe, court attachés, guards, priests, friends of plaintiff and of defendant, comprise the cast of this critical drama of law and of medicine 4000 years ago.

References

1. Toole, J. F., Ophthalmodynamometer. Arch. Int. Med., 112: 981, Dec. 1963.

2. Wood, F. A., and Toole, J. F., Carotid artery occlusion and its diagnosis by ophthalmodynamometer. J.A.M.A., 165: 1264, 1957.

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The Thiazide Drugs And Diabetes Mellitus

The usefulness of thiazide diuretics in the treatment of edema and hypertension is now definitely established. What we are beginning to find out after much careful observation are some of its side effects. Hyperuricemia and precipitation of Gout has been noted to be associated with thiazide administration since 1958.[1] Reduction of sodium concentration of extracellular fluid (hyponatremia) and depletion of body reserves of potassium (associated with hypokalemia) are complications which may arise in the course of therapy with any effective diuretic agent especially the thiazides. These alterations in the composition of the body fluids increase disability, may even interfere with reduction of edema and when severe jeopardize life. They can and should be avoided. If they occur they should be recognized and appropriately treated.

In the early studies of the use of thiazide drugs as diuretic and antihypertensive agents, it was noticed that several patients receiving these agents developed hyperglycemia. Then Goldner *et al*[2] studied the problem in a more systematic manner. Twenty non-diabetic subjects and a similar number of diabetic patients were given various diuretics by mouth. The non-diabetic group showed no elevation of blood sugar or change in glucose tolerance, while receiving thiazide, but six of the diabetic patients responded with an increase in the hyperglycemia and glycosuria. In another report Zatuchni *et al*[3] found that the post-prandial blood sugar increased in 14 of 25 patients suffering from cardiac disease, and Sugar[4] reported the development of diabetic acidosis in 2 pregnant diabetic women with the institution of thiazide therapy. Such reports are important in alerting the profession, since it is certain that a large number of diabetic or prediabetic patients receive thiazide diuretics for control of edematous states or hypertension for long periods of time.

The response of blood sugar to intravenous administered tolbutamide is a sensitive and reproducible method of evaluating carbohydrate changes. With this method Runyan[5] described new observations on the influence of thiazide diuretics on carbohydrate metabolism in patients with diabetes. He measured the response to I.V. administered tolbutamide and found that when the drug had been given in a large dosage for only seven days diabetes was affected adversely to a significant degree in 13 of 15 patients. When he employed a small dose the effect was much less or was even absent. Goldner noted a diabetogenic effect in his patients within 3-5 days after institution of therapy. In other cases longer periods have elapsed before the effects have been recognized. Patients with "potential" diabetes, that is those with a family history of diabetes and border-line abnormal glucose tolerance tests and elderly persons are more apt to be affected by the thiazide drugs than young non-diabetic persons.

The mechanism of the worsening is not understood. It seems not to be due to an increase in adrenal activity which could antagonize the insulin liberated by the pancreas. In mice a pancreatitis developed in 7.1 per cent when given chlorothiazide in doses comparable to that used in man.[6] But whether pancreatic damage is a factor in the altered carbohydrate tolerance in man is not at present known. It is clear enough that thiazide drugs can aggravate existing diabetes and activate latent diabetes, but there is at present no evidence that they can either cause diabetes or produce any permanent metabolic defect. This means that the effect of thiazide drugs on diabetes in clinical practice is seldom serious.

Generally in those cases in which thiazide drugs are definitely beneficial in the treatment of hypertension and edema, then continuance over long periods are practiced. It is in such cases where the physician must be alert to the need for appropriate adjustments of the diabetic regimen in order to maintain control of the hyperglycemia and glycosuria. It may become necessary to modify the diet and to begin to use or increase the dosage of insulin or the oral hypoglycemic agent. If both the patient and the physician are watchful then no harm may be expected to result. If the prudent physician is aware of the diabetogenic effect of thiazide drugs, he will make diagnostic tests for diabetes from time to time as a part of the routine follow up of such patients. What is especially heartening is that the diabetogenic effects of thiazide subside promptly with the discontinuance of the drug.

L.H.N.

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Digitalis And Neurotoxicity

An almost universal practice in a hospital, is the instruction to nurses to withhold the next digitalis dose if the patients pulse rate falls below 60. Implicit in this practice is the assumption that a pulse rate below 60 represents the first evidence of digitalis overdosage. But another assumption, one not explicitly stated, is that digitalis acts upon no other organs or tissues, or at least such action is not significant in appraising the level of digitalis action upon the heart. Neither of these assumptions is justifiable and if acted upon, can only lead to unproper use of this powerful and useful drug.

From the time that Withering introduced digitalis to the medical profession, there has been apparent a close relation between its neurotoxic and its cardiac effect. A wide variety of effects on the central nervous system have been described. Visual symptoms such as blurring of vision, yellow or green or flickering amblyopia and scotoma are well known and often precede toxic symptoms arising in the heart itself. Less well localized symptoms such as drowsiness, restlessness, weakness and headache may also occur. And only occasionally more extreme effects on the central nervous system such as hallucinations, seizures, delirium and even coma are also seen. Several authors have reported peripheral and trigeminal neuralgias and paresthesias. If we include anorexia, nausea, and vomiting (symptoms that occur even if the stomach is extirpated) in the estimation of the frequency of the effect on the central nervous system, then neurotoxicity is by far the most common manifestation of digitalis overdosage, and not the heart rate. What then should be considered the relationship between the cardiac effects of digitalis and the implications of neurotoxicity. Can one consider the signs of toxicity to digitalis in any organ a contraindication to its use or should neurotoxicity be ignored as it is being ignored in many hospitals and the drug given for greater therapeutic results until the heart itself gives the signal.

Lyon and DeGraff point out that two pharmacologic questions are implied in this confusion. One is whether there can be a significant dissociation between the neurotoxic and cardiotoxic effects. The other is whether an additional therapeutic effect is likely to be observed after the onset of neurotoxic symptoms. Answers to the first question involves some knowledge of the distribution of digitalis in the body. Studies with C14 labelled digitoxins, with tritiated digoxin and with unlabelled digitoxin by biaassay have shown that liver binds the largest amount and that very considerable amounts are found in the gastro intestinal tract and in the kidney. To be sure there are quantitative differences among the various methods of study, but one author reported that the heart bound only one per cent of an administered dose. Species differences have also been noted. Digitalis and its metabolites persist in the cat heart but little or no fixation is found in the rat heart. In short, digitalis is widely distributed throughout the body and there is no disproportiate amount in the heart.

In view of this wide distribution in the body and the species differences, it is not surprising that in the laboratory some variability in neurotoxic and cardiotoxic effects have been reported. Thus the presence of a sugar side chain on the cardiac glycoside consistently reduces neurotoxic effects. Remove the sugar component and one obtains a compound called digitoxigenin which produces convulsions in cats at doses in which digitoxins would be ineffective. On the other hand, digitoxin produces lethal cardiac toxicity in the same animal at a lower dose than does digitoxigenin. Similarly there are glycosides not derived from digitoxin that produce effects on the central nervous system only. In addition the animals that are insensitive to the cardiac effects of digitalis, such as the rat, can manifest neurotoxic effects primarily.

In man by contrast to what has been noted about differences among various animals, both laboratory and clinical evidence suggests that with the glycosides ordinarily used, the distribution of the drug and susceptibility to it are such that cardiotoxic and neurotoxic effects will occur with very similar doses of digitalis. Furthermore, deliberate digitalis intoxication in the same patient with the same glycoside might produce cardiac signs in one trial and central nervous system signs on the next.[1] It is clear that one cannot ignore the effects upon the central nervous system in order to await further therapeutic effects upon the heart, as the nurses instructions mentioned above assume. To do so can subject to the patient to a high risk of producing toxic arrhythmias. Apparently, the two effects of digitalis in man, neurotoxic and cardiotoxic, go hand in hand and if we wish to reduce the incidence of digitalis toxicity we must always think of neurotoxicity.

It is now possible to formulate a reasonable working hypothesis as to the mechanism or mechanisms of action to explain why the drug has both neurotoxic and cardiotoxic effects. The neurotoxic effects can be the result of a widespread action of digitalis upon cell membranes which interferes with the return of potassium ion into the cell during recovery. The cardiotoxic effect is intracellular and increases the contractility of actomyosin perhaps by increasing the calcium ion flux from the sarcolemma to the contractile element. If these hypotheses are correct, it would appear that all the effects of digitalis on the central nervous system are due to the membrane effect and are associated with intracellular depletion of potassium. The usual digitalis preparation produces its therapeutic contractility effect at doses at which no depletion of potassium can be measured even by subtle isotope techniques.

In most situations when neurotoxicity occurs, it can be assumed that a full therapeutic cardiac effect has already been achieved and therefore neurotoxic effects are a better measure of full digitalis action than waiting for cardiac signs, as nurses in hospitals are instructed to do. Furthermore, when there is marked intracellular depletion of potassium, such as one finds in severe chronic congestive heart failure, or after chronic use of diuretics then sensitization of the cell membrane to loss of potassium, makes it possible for neurotoxic symptoms to occur early. In this situation the neurotoxic effects are a warning of dangerous cardiac effects to come. In this case a greater therapeutic effect of digitalis can be achieved not by drugs that mark the neurotoxic effect, but rather by giving heed to them and adding oral amounts of potassium to the patients therapy.

L.H.N.

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Blood Letting In Coronary Disease

Years ago, blood letting was done indiscriminately for everything even for cholera, where hemoconcentration is extreme. No physiologic bases for this dogma were known and some great men in history such as George Washington were believed to have perished as a result of this senseless procedure. Perhaps this is the reason why there has remained a great reluctance to resort to phlebotomy when erythrocytosis complicates coronary heart disease, even though physiologic and rheologic considerations speak strongly in favor of this procedure.

There are many patients with myocardial infarction and or angina pectoris and ischemic heart disease that have erythrocytosis. In fact the Framingham group[1] has suggested that high levels of hemoglobin are associated with an increase in the incidence of coronary heart disease. Burch and DePasquale[2] have also observed over the past several years a high incidence of erythrocytosis in patients with myocardial infarction. In an effort to learn the relationship of hematocrit to myocardial infarction, the hematocrit levels of 100 men and 120 women with acute myocardial infarction were compared with those of age matched subjects without evidence of coronary artery disease. They found that the hemotocrit levels for the men and women with acute myocardial infarction were significantly higher than for those with the control subjects.

In general, coronary thrombosis is less common in patients with anemia than in patients with polycythemia. For one thing low erythrocyte concentrations are associated with lower levels of viscosity. Furthermore, mild anemia may even stimulate the formation of collateral circulation in the heart. Angina pectoris and myocardial infarction are extremely rare, to almost non-existent, in areas of the world where malnutrition, parasitic infection and chronic anemia are prevalent. On the other hand they are common in those areas where the population is well fed, plethoric and free from infections. There are many reasons other than hematocrit levels that render premenopausal women resistant to myocardial infarction as compared to postmenopausal women, but one factor may be related to low hematocrit levels found in premenopausal females and the "normal phlebotomies" of menstruation.

If erythrocytosis is one factor that predisposes a patient to myocardial infarction and angina pectoris, by what mechanism does it do this? Burch and De Pasquale believe that two factors are involved. One is its effect upon coronary blood flow past a narrow arterial segment and a second is its effect upon platelet adhesiveness. They point out that linear rates of blood flow for a given shear rate must decrease proximal to an area of narrowing in a diseased coronary artery. In segments with a slow rate of blood flow blood viscosity would increase. As the apparent viscosity of the blood

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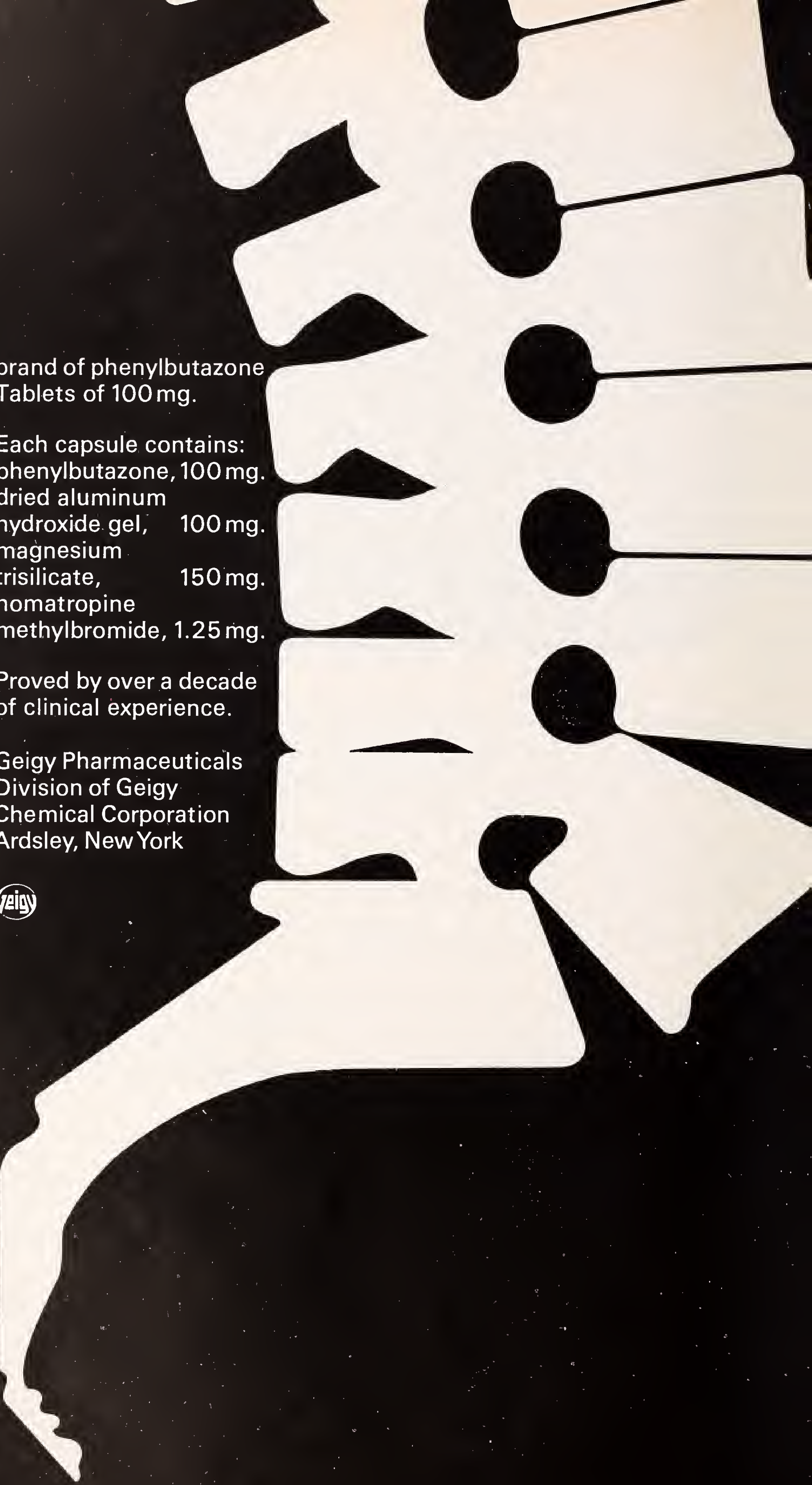

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increased, the energy necessary to force the blood past a narrowed segment of coronary artery also increases. Under such circumstances especially in the presenec of a diseased myocardium or a decline in arterial pressure there may develop local stasis or even cessation of blood flow. This could predispose to thrombus formation, but would also explain the frequent finding at autopsy of an infarcted area of myocardium even in the absence of coronary artery occlusion where blood stasis, not thrombus was the cause.

Certain characteristics of coronary blood flow may render the coronary arteries particularly vulnerable to an increase in hematocrit and blood viscosity. The maximal rate of blood flow occurs in the coronary arteries during diastole. During isometric contraction there is a sharp decrease in the rate of coronary flow and even backflow may develop at the height of myocardial tension. The changes in flow during a single cardiac cycle are much greater for the left coronary artery than for the right and as Burch and De Pasquale point out, during isometric contraction there develop an associated marked increase in apparent or manifested blood viscosity in the left coronary system. If this is so, it becomes understandable why an increased hematocrit may predispose a patient with atherosclerotic disease of the coronary arteries to angina pectoris or even myocardial infarction.

Another aspect of erythrocytosis is the relationship of hematocrit levels to platelet adhesiveness. Recently it has been shown[3] that the higher the hematocrit the more sticky are the platelets. Since coronary thrombi occur around "white" or platelet thrombi, the increased adhesiveness of platelets in patients with high hematocrits may explain why it is that myocardial infarction is prone to occur in patients with an elevated hemotocrit. To be sure, myocardial infarction may occur in the absence of thrombosis as a result of the stasis produced by partial obstruction of a coronary artery in the presence of a high hematocrit, as mentioned above.

It is necessary to realize that ischemic heart disease is a complex phenomenon and blood viscosity is only one of many factors which may be of importance. But a high hematocrit and a high viscosity deserve serious consideration in the management of ischemic heart disease if only because blood letting is an innocuous procedure that apparently can benefit patients. To lower the hematocrit would result in a decrease in cardiac work and would facilitate the flow of blood in arteries including the coronary arteries. All procedures in therapy aim to restore a given function of the body to its "normal state." Therefore, it is rational to attempt to reduce the hematocrit to normal or near normal values in patients with erythrocytosis and coronary heart disease by repeated phlebotomies of small volume. A recent practice described a group of patients with angina pectoris or acute myocardial infarction or both who had moderate erythrocytosis in whom a reduction of the hematocrit by phlebotomy decreased the frequency of anginal attacks in some patients. Burch and De Pasquale mention three male patients with the Tetralogy of Fallot age 32, 36 and 38 respectively in whom phlebotomy relieved the anginal symptoms in all three.

We now have a rational basis for venesection in patients with erythrocytosis and symptomatic ischemic heart disease. However, a more extensive study of the problem is necessary, for it is not known at what levels of hematocrit, phlebotomy is indicated and to what levels it should be reduced. It is known that certain patients with hematocrit over 50 per cent are benefitted by phlebotomy. It may even be desirable to reduce the hematocrit to 45 per cent by frequent small volume phlebolomies. Greater benefit may even be derived by lowering the hematocrit to 40 per cent to achieve levels common in menstruating women provided, of course, there is no pulmonary arteriocapillary block.

The therapeutic benefit of blood letting in erythrocytosis and coronary heart disease are clear for they were carried out in patients without polycythemia vera in which the benefits of blood letting are well-known and also in patients without pulmonary disease. Why it is that patients with coronary heart disease have a high incidence of erythrocytosis is not clear and needs further investigation. Do such patients suffer from increased psychic stress which is known to be followed by a marked sudden increase in the hematocrit. Perhaps it is associated with changes in renal blood flow and a resultant increase in erythropoiesis. These are still problems for further study. The benefit to be derived from reducing the hematocrit to normal in coronary heart disease however, is no longer in doubt.

L.H.N.

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Care Of The Unconscious Patient

Recently a young college student who had suffered critical brain damage in an auto accident, was interviewed five months later after he had returned to his college studies and was doing well.[1] Immediately following his accident he was unconscious and remained so for three weeks. His excellent recovery resulted in part because his body temperature was lowered to 88° F. (31.1° C) for a week thereby reducing the metabolism of the brain and its degree of reaction to the injury. But it was also made possible by the medical attendants who were aware of the body's normal protective mechanisms and had knowledge of how to substitute for them during the period of unconsciousness.

The normal patient during sleep, by moving, by sighing, by avoiding tracheal obstruction, by coughing up secretions, automatically protects himself.[2] The unconscious patient will have lost most, if not all, his normal protecting devices and in order to survive, he must depend on others to detect or anticipate his needs and institute appropriate measures to assure his recovery, if he himself can survive the immediate accidental or pathological insult.

There are several important tasks in caring for the unconscious patient, the most important one being to assure good pulmonary ventilation.[1] Eckenhoff points out the unreliability of using cyanosis as a sign of inadequate respiratory exchange.[3] To assure sufficient ventilation of an unconscious patient requires verification that the airways are patent and measuring the volume of respiration. The airway is best maintained if the patient is in the lateral position, and if this is not sufficient then resort to an endotracheal airway or tracheostomy becomes mandatory. Even then respiratory secretions may obstruct the artificial airways. Since an unconscious patient cannot rid himself of these secretions, they must be aspirated periodically for him with the aid of a sterile suction catheter.

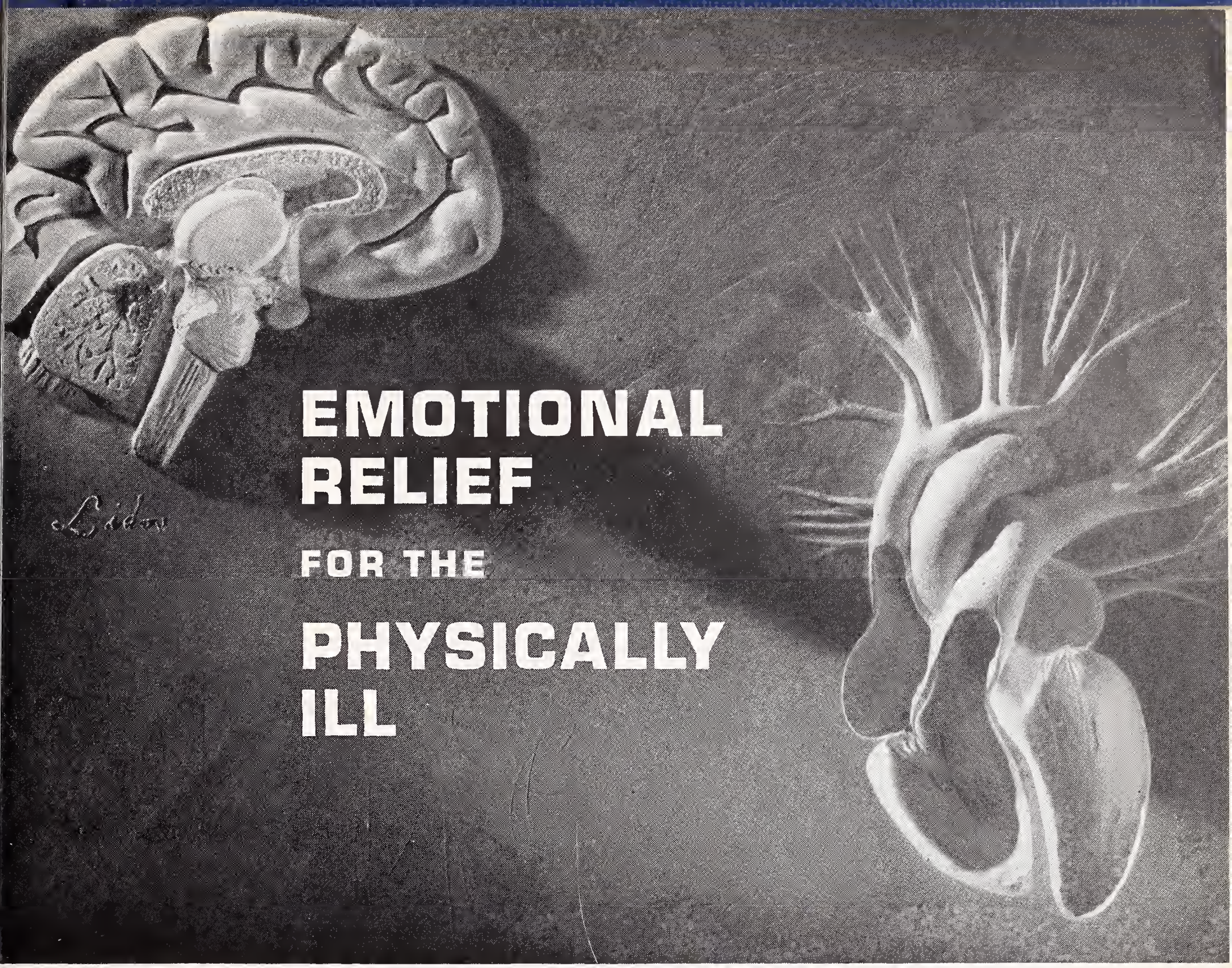
Eckenhoff believes it is probably wise to increase the inspired 0_2 content of all comatose patients, either by a properly placed naso-pharyngeal catheter with 0_2 flowing at 6 liters per minute, or by an oxygen tent. Occasionally however, such above normal oxygen concentrations may mask the existence of hypoventilation and hypercapnia which may enhance the coma. Co_2 can only be kept within normal limits if the alveolae are actively ventilated. If the patient is hypoventilating then, his respiration must be assisted by a respirator which preferably is triggered by the patients own rhythmic respiratory attempts.

There are several important gains from tracheostomy, but there are hazards also. At the beginning an endotracheal tube can be inserted through the mouth and adequate pulmonary ventilation obtained. If unconsciousness is expected to persist for more than several days, then tracheostomy will help to improve alveolar ventilation by reducing respiratory dead space, make it easy to remove respiratory secretions and if needed carry out artificial ventilation.

The hazards of tracheostomy must also be borne in mind. Most tracheas become infected soon after tracheostomy because of improper aspirating techniques. Such infection however, is preventable if only sterile catheters are employed for aspiration and are introduced by aseptic methods by the physician who has patience and takes time. The second hazard is insufficient humidification of inspired air. A tracheostomy bypasses the nasal cavity where the inspired air is warmed and moistened. Unless warm moistened air is offered to the patient there is danger of drying of respiratory mucus membranes, thickening of secretions, crusting and finally obstruction of air passages, circumstances that favor the development of pulmonary infections. One important point made by Eckenhoff is that bubbling of air or oxygen through a water bottle does little towards proper humidification.

The sleeping patient turns himself from one position to another thereby protecting himself against peripheral vascular stasis as well as pulmonary atalectasis.[1] Since the comatose patient cannot turn himself, his position must be altered hourly by his attendant and this should be accompanied by gentle back slapping to facilitate expulsion of secretions. However, turning must be accomplished with care, since often the sympathetic tone is diminished or lost during coma and hypotension may occur early when the body position is changed rapidly or during transportation. This kind of a complication is especially likely to occur in the presence of blood loss. Turning therefore, should be preceded and followed by observation of blood pressure response.

It is self evident to strive to maintain the circulation by combatting shock and supporting the blood pressure in a coma patient. However, certain questions always arise requiring answers that vary from patient to patient. Since body metabolism is reduced during unconsciousness, the demand for blood is thereby lessened, and if hypothermia is employed, this is especially so. What then should the blood pressure level be maintained at? Should we attempt to maintain a comatose patient's blood pressure at levels normal for the conscious patient by the use of pressor substances. This is not physiologically sound. Clearly judgments will constantly



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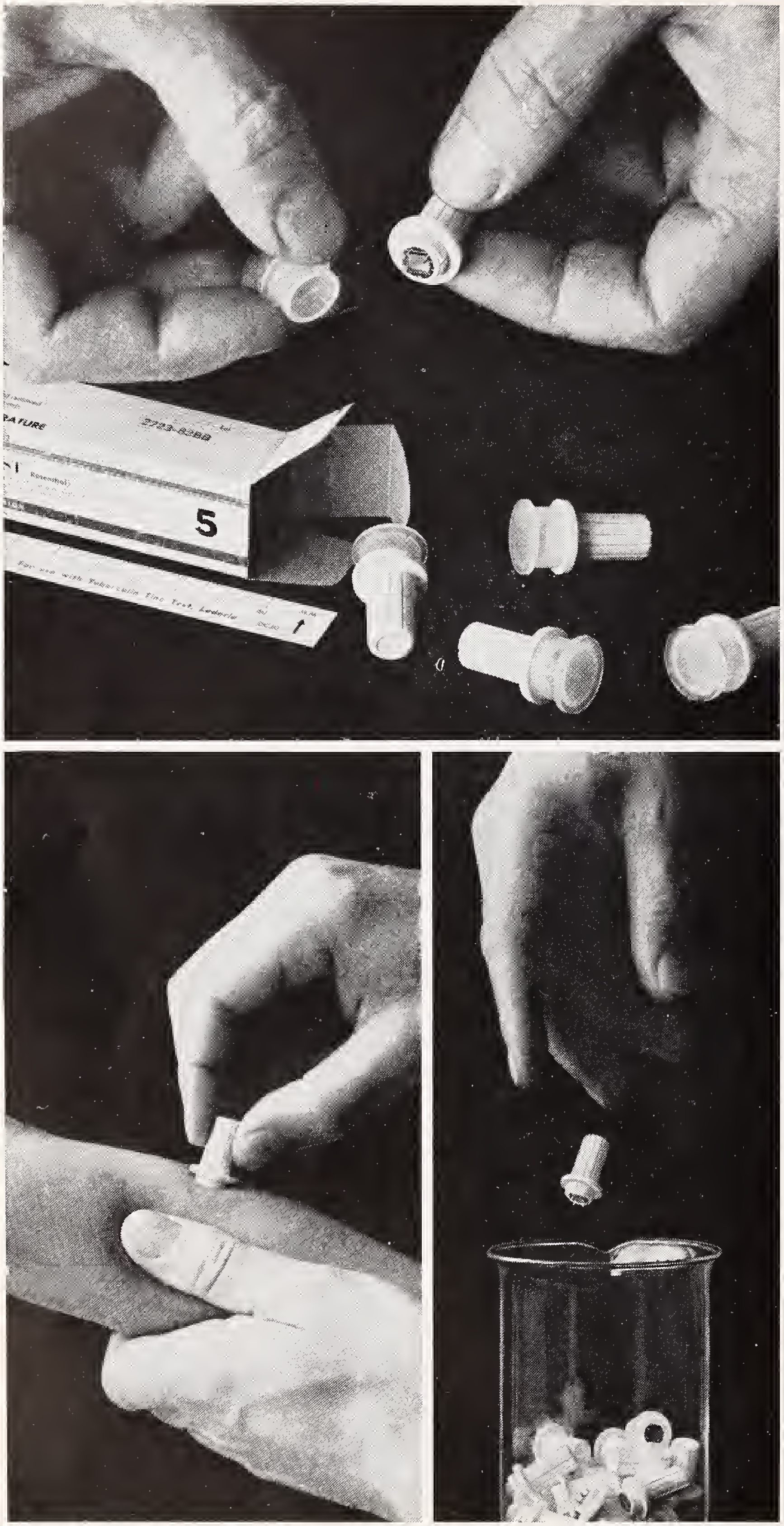

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If a patient is unconscious because of a stroke or cerebral trauma, it is important to prevent accumulation of CO_2 in the blood for this ion has a well known dilator effect on cerebral circulation. It also leads to elevation of cerebrospinal fluid pressure. In the face of dilated cerebral vessels and if there is also an elevated blood pressure, the brain volume will increase and predispose to cerebral edema. Thus it would appear that hyperventilation by blowing off excess CO_2 might be desirable to achieve a reduction in cerebral volume and cerebral blood flow.

Brain damage after trauma can be minimized by lowering body temperature to 86-88° F. for several days after injury. Since body metabolism is directly related to body temperature, 0_2 utilization and demands for blood flow increase should be prevented by use of cooling blankets and other appropriate means. This is especially mandatory if fever occurs. While this is now a common technique in the treatment of trauma and cerebral aneurysm, it also deserves a trial in the treatment of strokes per se, since here also cerebral edema, high cerebrospinal fluid pressure and fever may occur. Theoretically it should be of value and deserves further explanation. Failure to consider the cerebral circulation in physiological terms will reduce the opportunity for recovery and may increase the extent of infarction and the degree of residual paralysis.

Careful attention to many minor details such as care of the bladder by indwelling catheter, care of the skin, of the eyes, of oral hygiene, passive exercise of the extremities to preserve the peripheral circulation and normal muscle tone are also keys to success.

There appear to be no magic tricks or drugs in the care of the unconscious. Primarily, what is required is to imitate the body's own protective devices. The basic attempts are to achieve adequate pulmonary ventilation, to keep the cerebral blood flow adequate, to offer the patient an appropriately controlled temperature and to protect the body both from within and without.

L.H.N.

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The Periodic Deep Breath

Periodic deep breathing is a natural phenomenon familiar to all of us who have observed the deep sighs taken by most people in waking life. Since this phenomenon is universal, it would suggest that it plays an important role in regulating the carbon dioxide and oxygen tension of the arterial blood. One would suspect that without the periodic deep breath or sigh, the normal tidal ventilation of the lungs might be inadequate to provide inflation of all parts of the lungs. Animal experiments have borne out this hypothesis. Mead and Collier[1] found that a constant ventilating tidal volume led to a progressive decrease in pulmonary compliance (distensibility) unless periodic deep breaths were supplied. In man also this phenomenon occurs, since Ferris and Pollard[2] demonstrated that unless a periodic deep breath is taken, pulmonary compliance decreases progressively during ventilation. Such changes take place both during spontaneous breathing and when ventilation is supplied by mechanical means. It would appear as the pressure and volumes used during normal ventilation are not high enough to keep all areas of the lungs adequately inflated.

One could suppose that with every return of the lungs to the resting and expiratory position some alveoli collapse and stay so, and periodically higher pressures are needed to open a completely collapsed air space than to inflate further one already partially filled with air. If this hypothesis is true, then tidal breathing should be associated with progressive atelectasis and the periodic deep breath (or sigh) employs pressures and volumes sufficient to reopen collapsed air spaces and thus reverse the progressive atelectasis.

Bendixin *et al*[3] report the clinical consequences of an artificially supplied fixed ventilatory volume in man. They studied eighteen patients without known pulmonary disease coming to operation for procedures requiring profound muscular relaxation and controlled ventilation. They observed that ventilation varies from case to case, from moderate hypoventilation to outright hyperventilation. However, when the ventilation remained constant as defined by arterial CO_2 and O_2 tension, then changes did occur in arterial O_2 tension and in total pulmonary distensibility. There was an average fall in arterial saturation of 22 per cent. In patients with hyperventilation the fall in arterial oxygen tension was small, but with normal or less than normal ventilation the reduction of arterial oxygen tension was significant. In these patients repeated hyperinflation produced a step-wise rise in oxygen tension and further improvement resulted from each successive inflation. Distensibility of the lungs returned to normal after the first inflation.

This fall in arterial oxygen tension which these authors observed during constant ventilation supports the hypothesis that the ventilatory pattern alone can lead to atelectasis and shunting of unoxygenated blood into the arterial side. As atelectasis develops during constant ventilation, there develops side by side a reduction in total pulmonary distensibility with a return to control values by hyper inflation. Atelectasis seems to develop regardless of whether pure oxygen or air mixtures are used.

The finding of a relation between the degree of ventilation and the magnitude of fall in arterial oxygen tension is of considerable clinical importance for it indicates that purely mechanical collapse of alveoli without superimposed infection can take place at any time during or after operation. The high incidence of clinical atelectasis and pneumonia after thoracic and high abdominal operations and the reports on post operative hypoxia after the same procedures points to factors that interfere with periodic hyperinflation of the lungs. Prolonged effects of anesthetics, certain positions and restrictive bandages are all possible factors in limiting the adequate expansion of the lungs, thus leading to atelectasis. It must further be remembered that spontaneous deep breaths do not occur during general anesthesia and that both pain and morphine inhibit spontaneous deep breathing in post-operative patients.

The lesson to be learned from animal studies and also from Bendixin's observations on patients is that the atelectasis caused by absence of occasional hyperinflation of the lungs, can be prevented and that what seems to be adequate ventilation may not be so. The low values of oxygen tension that can develop after an hour of constant breathing suggests that anesthetists should use nitrous oxide and oxygen in ratios higher than 3:1. There is a possibility that patients in recovery phase will be inadequately oxygenated when breathing room air not because of hypoventilation in the accepted sense but because they are unable to take deep breaths periodically. Furthermore, deficient oxygenation is bound to be injurious particularly for the patient who requires the ventilation most, the pulmonary or the circulatory cripple. Most important however, is the need to revise our current thinking about atelectasis. It appears to occur quickly long before any X-Ray recognition of its presence, if constant regular ventilation of the lungs takes place without frequent periods of hyperinflation.

Now that we recognize the importance of a treatment as vital as pulmonary ventilation, it seems appropriate to develop habits of testing growing oxygen unsaturation not by clinical impression alone, but by some manner of objective measurement. There are now available simple and relatively inexpensive apparatus for measuring pH and blood gases. Furthermore, automatic respirators cannot at present measure pulmonary ventilation. Few if any machines meet the requirements, to be able to counter loss of pulmonary compliance due to a fixed ventilator volume by a compensatory increase in inflating pressure. The skilled hand of the anesthesiologist is still needed for periodic hyperinflation.

An instrument needs to be devised which by some feedback system will operate as admirably as does the normal physiologic control of respiration and circulation.

L.H.N.

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Decisions By "Mere Mortals" At FDA

As an alumnus of the Food and Drug Administration, I have a friendly feeling toward that organization. Despite that I must oppose the unlimited power it is seeking over medical matters and matters of opinion. I cannot forget that the first chief of the Food and Drug Administration started out wrong on the toxicity of saccharin and benzoate of soda. His successors from top to bottom being mere mortals will inevitably be wrong many times again. The progress of medicine, the development of new and better tools for our physicians is a cause that makes it critically urgent that there be more ample opportunity for review by and appeal to others of decisions of this agency—Theodore G. Klumpp, M.D., in *Journal of New Drugs,* July-August 1963.

Total Pneumonectomy: Some Historical, Physiologic And Clinical Considerations*

Gustaf E. Lindskog, M.D.†

■ A distinguished American surgeon wrote in 1939:[1] "The accomplishment of pneumonectomy in man will stand out as one of the great surgical contributions of the present decade." Today pulmonary resection in one of its several forms is commonplace and overshadowed by open-heart procedures. Most of these technical advancements have occurred within the past three decades, although Gluck[2] and Bloch[3] demonstrated the feasibility of pulmonary resection in the experimental laboratory as early as 1881. Sporadic attempts to eradicate a cancerous lung in humans were made by several surgeons, notably Kummel (1910) but met with failure for a number of reasons to be discussed later.

The first successful *subtotal* pneumonectomy was described by Rudolf Nissen,[4] Sauerbruch's first assistant, in 1931, employing the mass ligature method. His patient was a girl with total bronchiectasis of the left lung, developing after trauma and probably related to a fractured bronchus. A second very similar case was reported by Haight[5] of Ann Arbor in 1934. Again the technic was a two-stage procedure, and the result was satisfactory after a protracted convalescence.

The first successful *subtotal* pneumonectomy for cancer was performed by Evarts Graham of St. Louis in 1933.[6] The patient was himself a physician, and the lesion was determined to be malignant by bronchoscopic biopsy. The operation intended was a left upper lobectomy, but technical considerations required a subtotal pneumonectomy. This was performed by mass ligation, and followed immediately by a partial upper thoracoplasty which was converted to total thoracoplasty after several weeks when the expected bronchopleural fistula and empyema ensued. The patient made a happy recovery and actually outlived his surgeon, who died of the same disease, with the treatment of which his name will forever be remembered.

In the same year, 1933, Rienhoff[7] of Baltimore reported two *total* pneumonectomies for neoplasms, one in a young child. Each was completed in a single-stage operation during which the main artery, veins and bronchus were identified, dissected free, and individually sutured. The closure of the chest was accomplished without drainage of the pleural space or thoracoplasty. When Overholt[1] reported a series of 22 pneumonectomies in 1939, it included 5 postoperative deaths or 22 per cent; the mortality in the 104 cases he was able to gather from the litertaure was a forbidding 49 or 47 per cent, and 65 per cent in those operations where the lesion was malignant.

What were some of the obstacles to be overcome and some of the dreaded complications which led to these discouraging early results? Obviously one of the most important was a necessarily smooth and safe open chest anesthesia. Ferdinand Sauerbruch, working in von Mikulicz's clinic in Breslau at the turn of the century, had tried to resolve this problem by a very cumbersome method — using a negative-pressure chamber ("Unterdruckskammer"). In this method, the operating room became in effect a giant respirator under slightly negative pressure; the patient's airway was exposed to normal ambient pressures by extruding the head through a rubber-collared port in the wall of the pressure chamber. This awkward solution was physiologically sound, perhaps even ideally so but highly impractical. At least one *Unterdruckskammer* was built and operated in this country, at the old German Hospital in New York (now Lenox Hill). The reverse solution, endotracheal positive pressure breathing, was developed by the internist Meltzer,[8] also of New York about 1909. It was rapidly popularized by early anesthesiologists and today is standard procedure for open chest operations and many others.

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Another technical problem, and perhaps a somewhat exaggerated one, was to conduct safe dissection in the pulmonary hilum where the individual vessels might be one to three centimeters in diameter, particularly when normal cleavage planes were obliterated by infection, fibrous adhesions, or malignant tissue. This obstacle was overcome, as previously stated by Reinhoff[7] at Hopkins for total pneumonectomy, by Churchill (1939),[9] and Blades and Kent (1941),[10] among many others for lobectomy and segmental resection. After 1941, almost all resections were being conducted in an anatomical fashion, with individual suture of the vessels and bronchi. Today this is standard procedure from which one rarely if ever departs.

Still a third problem was the management of the hemithoracic space remaining after ablation of an entire lung. As is so often the case with progress in surgery, the early experimental work pointed the way to a correct solution—single stage excision of the lung with primary closure of the chest. However, these experiments did not appear directly applicable to the human case; under conditions of mass ligation through an infected pulmonary hilum the incidence of postoperative bronchopleural fistula was very high. Drainage of the usual empyema and secondary thoracoplasty appeared to be routinely necessary, as exemplified by Graham's successful case in 1933.

The volume of one adult human lung, or rather its air content at the maximal expiratory level, is in the range of 1200 to 1500 ml. How does the body compensate for this space remaining after total pneumonectomy? A study of post-pneumonectomy X-rays suggests several answers—contraction of the bony framework, narrowing of interspaces, elevation of the hemidiaphragm, progressive shift of the media stinum toward the operated side, and herniation of the remaining lung. The herniation involves chiefly the anterior segment of the upper lobe, substernally through the anterior mediastinum, which is normally a thin area. A lower site of herniation exists behind the heart and esophagus in front of the vertebral column. The above readjustments, which are all strictly mechanical, may reduce the residual hemithoracic space to a mere 150 or 200 cubic centimeters. Finally this space is occupied entirely or partly by transudated plasma, fibrin, and eventually fibrous tissue. The space then comes to have the appearance of a mesothelial-lined polycyst.

Much attention has been devoted to the nature of enlargement in the remaining (contralateral) lung. Is this simply hypertrophy—i.e., an expansion of pre-existing partly collapsed alveoli and lengthening of the alveolar ducts, or is there an element of hyperplasia? There is little doubt at present that in the adult human the process is hypertrophic. In the very young, and in certain animals whose growth potential remains high into adult life (e.g. the rat) there is evidence of proliferation of alveoli and ductules in the studies carried out by Hilber[11] in Germany and Bremer[12] at Harvard. As a result in the young subject the average size of alveoli remains small in the residual lung.

A fourth and entirely technical problem was the proper method of closing the bronchial stump after its transection. Efforts to reduce the incidence of bronchopleural fistula with its dire consequences led to some ingenious, and some later unnecessary, experiments. The early work of Rienhoff showed that healing of a major bronchus was frequently by secondary intention and that it was only essential to obtain an airtight closure during the period when an inflammatory barrier was being established in the peribronchial tissues of the mediastinum. It was soon apparent that simple circular ligature was inadequate to accomplish this objective except with the smallest of bronchial radicles. The large bronchi are too inflexible because of their cartilaginous structure; ligatures tended to break or erode and lumina reopened. A careful, single-layer, interrupted end-on closure employing nonabsorbable suture material like silk or cotton was proved best, when care was taken to approximate the membranous posterior wall accurately to the inner circumference of the cartilage ring. Reinforcement of the bronchial suture line with a pedicled flap of pleura and lung, or even a simple flap of pleura is an additional safeguard. Excision of one or more of the distal cartilage rings has been attempted to permit better collapse of the bronchial stump and closure, but this is technically difficult and adds no measurable improvement. Prosthetic plugs or cylinders of metal or plastic have also been evaluated, but these may subsequently erode into the bronchus or pleura. In summary, the criteria for good bronchial healing are a meticulous and immediately airtight closure using multiple interrupted nonabsorbable sutures, an intact bronchial arterial supply, a short stump deeply buried in the mediastinum and/or covered with a reinforcing pedicled flap of pleura or pulmonary tissue.

Physiologic Considerations

In the early postoperative period after any type of pulmonary resection, there is a considerable but reversible loss of ventilatory function based on wound pain, pleural effusion, pneumothorax, trauma to the musculature, and altered pulmonary compliance caused by infection and edema. Heavy sedation may contribute further to hypoventilation, hypoxia, and hypercapnia. Therefore, many patients show some degree of respiratory acidosis during and after surgery. This derangement is usually self-limited due to correction of, or spontaneous improvement in, the above causative factors and to metabolic readjustments such as chloride excretion and increased bicarbonate formation.

The MBC (maximum breathing capacity) and the WMV (walking minute ventilation of Warring)[13] are useful indices in evaluating patients' ability to tolerate pneumonectomy. Obviously, a great deal depends on the age of the subject, the presence or absence of cardiac disease, the presence or absence of diffuse bronchial disease and the functional state of the lung to be removed. If the diseased lung is totally obstructed and atelectatic, already destroyed by disease, encased in a restraining pachypleuritis, or collapsed under thoracoplasty, its excision is not likely to reduce much further the patient's ventilatory reserve after the immediate postoperative adjustment. Indeed, pneumonectomy may result in a net improvement of function. An initially low or borderline MBC in the stiuations just enumerated has less significance than when both the lungs are functionally more nearly equal. In general, however, one has concern when an MBC falls below 70 to 75 per cent of the calculated normal especially when the walking minute ventilation is high and the ratio of WMV/MBC is above 35 per cent. Yet total pneumonectomy has been well tolerated by patients with MBC's around 45 or 50. Some of these require tracheostomy and positive pressure breathing as described and practised by Björk and Engström,[14] to tide them over the postoperative period with its inevitable restriction in ventilation. At the first signs of ventilatory insufficiency and a rise in the arterial pCO_2 one should not hesitate to resort to tracheostomy.

An immediate effect of pneumonectomy, or more specifically ligation of the main pulmonary artery, is a sudden increase of pulmonary arterial pressure because there is an increase in blood flow to the one remaining lung, and the expansion of its peripheral vascular field takes time to develop. According to Scarff[15] this increased pressure may be as much as 30 to 50 per cent of the systolic, slowly reducing itself in 7 to 20 days.

The first study of the functional response to total pneumonectomy was carried out by Heuer and Andrus[16] in 1922. They employed anesthetized animals at rest and, therefore, did not observe the effects of exercise. They demonstrated 1. an increase in alveolar CO_2 lasting up to 30 days and a slight increase in arterial pCO_2; 2. a decrease in alveolar O_2 lasting from 28 to 66 days, and a marked fall in arterial pO_2 for at least 11 days.

Longacre,[17] working in Carter's laboratory, went a step further and studied the response of young and trained dogs to measured treadmill exercise before, and two to five months after, pneumonectomy. A one-hour run of 2300 M, (1.4 miles) caused some elevation in body temperature and pulse in the normal animal. After total pneumonectomy the temperature rise was doubled, and the pulse acceleration tripled but there was no demonstrable arterial oxygen desaturation. After a one and one-half hour run on the treadmill (3450 M.) there was marked desaturation of the arterial blood, becoming less severe with each succeeding trial run. In the two-hour test run of 4600 M. there ensued severe dyspnoea, an alarming rise in pulse and respiratory rates with marked desaturation in the peripheral arterial blood which also tended to diminish with successive monthly testing.

In the human sphere, Lester, Cournand and Riley[18] studied three children aged 9, 12 and 14, several years after left total pneumonectomy for suppurative disease. All demonstrated normal hemoglobin levels, and arterial oxygen saturation; two of the three had normal ventilatory tests. One with a very marked mediastinal shift and overdistention of the remaining lung showed a lowered vital capacity and MBC with an elevated functional residual (subtidal) volume.

Cournand and his associates[19] published in 1950 a classical paper on this subject, recording both early and late observations after pneumonectomy. The early group comprised seven individuals studied from one to five months after surgery. The writers found that the average size of the remaining lung at the height of inspiration was only slightly increased but was 50 per cent greater at forced expiration. Therefore the ratio of residual to total air was increased. The MBC averaged 63 per cent of normal. There was slight hyperventilation. The breathing reserve was 45 per cent of normal. The mean values for arterial oxygen tension were normal at rest and slightly reduced after one minute of exercise. The alveolar-arterial O_2 gradient was normal while breathing 12 per cent oxygen. The total pulmonary arterial flow and the pulmonary arterial pressures were normal in the two cases where these parameters were determined.

Cournand's second group consisted of nine cases, studied from 25 to 131 months after pneumonectomy (averaging 77 months). The patients' ages ranged from 17 to 72. The average size of the remaining lung was 125 per cent of the predicted normal at inspiration and 175 per cent at the forced expiration level. The MBC was 70 per cent of the predicted normal. The breathing reserve during standard exercise test averaged 53 liters, and 47 L. one minute after exercise, both 60 per cent of normal. The oxygen consumption was normal. The arterial oxygen saturation was normal at rest and slightly diminished after exercise. The alveolar-arterial O_2 gradient was likewise normal while breathing 12 per cent oxygen. The pulmonary arterial pressures rose from an average of 15 mm. Hg. at rest to 24 mm. Hg. after exercise. However, Cournand's data clearly showed that the mean pulmonary arterial pressure rose above an average of 15 mm. Hg. in the post-pneumonectomy state only when the pulmonary flow exceeded 5.0 L./min./sq.M. body surface, provided the remaining lung was essentially normal. However, among 5 emphysematous patients the pressures were elevated (18 to 32 mm.) at flows of 3.0 L./min./sq.M. after pneumonectomy.

One may conclude then from clinical, physiologic and experimental observations that the adjustment to total ablation of one lung may be very satisfactory, sometimes indeed nearly perfect. The following factors have a favorable influence on the adjustment: 1. youthfulness of the patient, 2. absence of degenerative or inflammatory disease in the remaining lung, 3. stability of the mediastinum, 4. recovery from operation without complications, 5. passage of time after surgery, 6. good physical tone and muscular conditioning. Nevertheless, there is a critical level of exercise in any case beyond which decompensation begins, the pulmonary arterial pressure rises, arterial oxygen saturation declines and the related symptoms and physical signs appear.

Morbidity And Mortality

A review of available reports concerning pneumonectomy for bronchogenic carcinoma reveals operative mortalities ranging from about five to twenty-five per cent. The New Haven Hospital experience in the first 145 resections included 20 postoperative deaths or 13.8 per cent. These data included, of course, the very earliest case experiences. When one compared the mortality of pneumonectomy with lobectomy there was a striking divergence (as in all series). Twenty-four lobectomies for cancer had one operative fatality or 4.2 per cent, as contrasted with 19 deaths in 121 pneumonectomies or 15.7 per cent. The results are undoubtedly much improved in the present decade.

Left pneumonectomy carries a consistently lower mortality than right because it is technically simpler, the incidence of bronchopleural fistula is less and the left is the smaller of the two lungs (in the ratio of 55/45).

Causes of morbidity and mortality are tabulated in an accompanying chart (Table I). The first six categories — bronchial fistula with empyema, cardiac arrest, major hemorrhage, hemopericardium, mediastinitis, and obstruction of the superior vena cava with acute cerebral edema may be considered as initiated by, or related to, technical inadequacies. The remaining five categories, comprising 12 of the 20 deaths can be ascribed to pre-existing or concomitant infection and cardiovascular disease. Significantly, *occlusive* vascular disease was responsible for six of the 20 fatal outcomes, and it was an important cause of postoperative morbidity in some surviving cases. Total pneumonectomy, therefore, is not to be employed lightly in the elderly patient with malignancy. It is safer to perform lobectomy or bilobectomy whenever the location of the primary lesion and the extent of local tissue or lymphatic permeation will permit. It is wise never to carry out total pneumonectomy without a preliminary tissue or cytologic diagnosis.

TABLE I

CAUSES OF MORTALITY IN PNEUMONECTOMY FOR CANCER

Bronchopleural fistula and empyema	1
Cardiac arrest during anesthesia	2
Hemopericardium and tamponade	1
Hemorrhage from major vessel	2
Mediastinitis	1
Obstruction of superior vena cava	1
Cardiac failure and pulmonary edema	3
Pneumonitis, bacterial	3
Pulmonary embolism	2
Cerebral vascular occlusion	3
Coronary thrombosis	1
Total	20

In comparing the mortality rates of total pneumonectomy performed for infectious disease with those for neoplasm, it is not surprising to find that the immediate (as well as the late results) are much more favorable in the former, probably because one deals with a relatively younger group of patients harboring less comcomitant cardiac and peripheral vascular or degenerative pulmonary changes. Between the years 1934 and 1953 at least 47 pneumonectomies (including several pleuropneumonectomies) were performed on the University Service of the New Haven Hospital in the treatment of advanced pulmonary tuberculosis. There were no deaths, and only three deaths occurred among 88 resections of lesser extent.[20] Similarly, there were no postoperative fatalities among 14 pneumonectomies performed in cases of bronchiectasis during the period 1937-52 as reported by Hubbell[21] on the same hospital service.

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Congenital Heart Disease

Cardiac malformations have been noted since the first treatise devoted to heart disease, Senac's *Traité de la structure du coeur, de son action et ses maladies,* published in 1749, in which a case of complete absence of the interventricular septum was recorded, the cyanosis being explained as due to admixture of venous and arterial blood, and the time of Morgagni (1761) who reported pulmonary stenosis and ascribed the cyanosis to venous stasis. Bouillaud (1835) recognized the two origins—arrest of development and foetal endocarditis; Hope (1834) believed that far the most frequent cause was a defect or premature cessation in the process of development, but it was not until 1906 that the cause of congenital heart disease was shown by Keith to be due, in the majority of cases, to an arrest of development of the bulbus cordis, and not to foetal endocarditis, as suggested by Kreysig (1817) and urged by Rokitansky. The morbid anatomy of congenital heart lesions was specially investigated by Louis, Bouillaud, Peacock (1858), Rokitansky (1875), and Maude Abbott (1908).—Sir Humphry Davy Rolleston. *The Harveian Oration.* Great Britain, Cambridge University Press, 1928, p. 38.

Radioisotopes In The Study Of Renal Function*

Richard P. Spencer, M.D.

■ The kidneys, lying within the perirenal fat mass, are hidden from direct observation except at times of operative intervention (or to a limited extent, through the use of renal biopsy). To evaluate renal appearance and function, a number of procedures have been devised (Table I). These techniques have recently been supplemented by radioisotopic methods. It will be recalled that many of the conventional studies of the kidneys are not without risk. For example, the intravenous pyelogram carries the possibility of patient reaction to the compound, and also saturates the body with iodine for many months. Radioisotope studies of the kidneys, which avoid these difficulties, may be useful as screening procedures. Further, as will be pointed out, the radioisotope techniques often supply information that cannot be obtained by other methodologies.

TABLE I

CONVENTIONAL STUDIES USED IN EVALUATION OF THE RENAL APPARATUS.

MORPHOLOGY	
	Operation
	Biopsy
	Perirenal air insufflation
	Retrograde pyelogram
	Aortography
FUNCTION	
	Intravenous pyelogram
	Catheterization
	Clearance studies
	Urinalysis

Estimation Of Residual Urine In The Bladder

After formation of urine through participation of glomeruli and tubules, urine collects in the bladder prior to its discharge. Bladder disease, or disorders of the outflow tract, can be accompanied by urinary retention. Such retention in turn may further impair the urinary tract. The conventional approach to determining the extent of urine retention in the bladder has been to perform urethral catheterization. However, catheterization is accompanied by irritation, and occasionally even infection. Any procedure that reduced the need for catheterization would be a useful addition. Mulrow and co-workers[1, 2] introduced a method for the radioisotopic determination of residual urine, which obviated the need for catheterization in many instances.

The basis of this study is the fact that, with normal renal function, several organic compounds containing iodine are passed (nearly quantitatively) from the blood stream into the urine. In other words, one-to-three hours after their intravenous injection, they should reside in the urine. These substances can be produced with radioactive iodine (I^{131}, half-life 8.1 days, principal emission a 0.36 MEV gamma ray) in place of the stable iodine. The compound of choice would appear to be o-iodohippuric acid (known by the trade name of Hippuran). Using a standard scintillation probe, placed about 20 cm. from the bladder, radioactivity is determined several hours after intravenous injection. A count over the precordium is used to correct for radioactivity that is in the body, but not in the bladder. The patient then voids as much urine as possible, and its volume is noted. Counts are then taken over the bladder again. The following simple relationship is employed:

$$\underset{\text{volume}}{\text{Residual bladder}} = \frac{\text{volume voided}}{\text{counts voided}} \text{ x } \underset{\text{over bladder}}{\text{residual counts}}$$

The initial studies showed good correlation between this procedure and drainage instituted by catheter.[1, 2] Hence, radioisotopic determination of residual urine can be employed first as the procedure of choice, and may make catheterization of the patient unnecessary.

Scanning Of The Urinary Bladder

The urinary bladder filled with 400 ml. fluid corresponds to a sphere of about 4.6 cm. radius. When such a sphere is filled with gamma-emitting radioactive fluid, it can be scanned by conventional techniques. We are in the early stages of gathering data on this procedure, but it appears to have value in the differential diagnosis of suprapubic

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masses, in bladder compression due to abdominal tumors, and in following the size of bladder tumors which project into the lumen.

Renal Localization And Scanning For Space-Occupying Lesions

Since certain I^{131}-labeled dyes are excreted by the kidneys, they can be used to study the size and location of the kidneys, as well as the presence of larger space-occupying lesions, through use of external scanning.[3] Scintillation scanning of these I^{131}-dyes is complicated by the fact that the materials have but a short residence in the kidney and their accumulation depends upon adequate renal function; hence, the timing of the scan after administration of the compound must be optimal. The quantity of stable (nonradioactive) compound administered is on the order of only a fraction of a milligram. Hence, allergic responses are rare, and, in addition, the body is not overloaded with iodine.

Mercurial diuretics, including chlormerodrin, concentrate primarily in the renal tubules.[19] It is possible to synthesize this diuretic with Hg^{203}. Since Hg^{203} has a usable half-life (about 46 days) and a medium energy gamma emission (0.28 MEV), it can be employed to obtain external scans of radioisotope localization in the kidneys. Space-occupying lesions of the kidneys, such as infarcted regions, abscesses, or tumors, usually fail to take up the radiolabeled diuretic. Hence, they can be detected as regions of decreased or absent accumulation of radioactivity.[3] The half time of Hg^{203} in the body is on the order of only three hours, since the diuretic is readily excreted. Hence, the radiation dose delivered to the kidneys is not excessive and the study can usually be repeated as necessary. Since the test depends on binding of the diuretic agent to the kidneys, it can be used in cases of mild uremia, when the intravenous pyelogram would be of little value.

There are several variations of the technique that are useful:

1. Bilateral scans of the kidneys can be superimposed on an abdominal radiograph, in order to obtain better anatomic localization.[4]

2. Repeated rapid scanning of the kidneys can be performed to follow the time course of localization of the radioisotope. A device being perfected by Dr. Merrill Bender (Roswell Park Memorial Institute), termed the autofluoroscope, permits the time course of events to be followed, and may enable the renal cortex to be distinguished from the medulla.

3. The rate of accumulation of chlormerodrin-Hg^{203} at two points in time, in each kidney, can be employed as an index to compare activity of the right and left kidneys.[5]

4. Experimentally, we have found chlormerodrin-Hg^{203} to be of use in delineating the size and location of the kidneys in animals as they develop. That is, changes can be followed as the animal grows and matures.

Radioisotope Renogram

Since various I^{131}-dyes are excreted by the kidneys (some by glomerular filtration, others through participation of the tubules as well), a means is at hand for following renal dynamics at a fixed point (as opposed to scanning over the kidneys). Administration of such a compound, followed by measurement of radioactivity as a function of time has been termed the radioisotope renogram.[6] Recently radiolabeled Hippuran has been utilized, as the substance administered intravenously, because of its almost quantitative excretion into the urine (without hepatic uptake). A typical dose of 50 microcuries delivers less than 10 milliroentgens of radiation to the patient, since the compound is rapidly cleared by the normal renal system (the half time of the radiolabeled Hippuran in the blood stream is on the order of 10 minutes).

The patient is seated in a comfortable position, such as leaning over a table. Identical probes are located over the kidneys (the kidneys may previously have been identified by X-ray),[7] and are attached to count rate meters and recorders. The probes are usually well shielded so as to reduce radiation picked up from the contralateral kidney. However, excessive collimation will allow focus on only one point and will miss the overall performance of the kidney. Following intravenous administration, there is a brief time lag until the radioactive bolus arrives at the kidney. Activity then increases rapidly, as Hippuran is extracted from the blood and is transferred into the renal tissue and over into the urine. Absence of the kidney is, of course, associated with little increase in activity over the renal area (there is some as the bolus enters the renal artery). Absence of free flow of urine down the ureters is associated with an increase in activity with no significant subsequent fall; hence, partial or complete ureteral obstruction is usually readily diagnosed by the radioisotope renogram. By itself, the procedure may give little indication as to intrarenal blood flow, but the two kidneys can be compared.

Many ideas have been advanced to explain the significance of the curve of the radioisotope renogram. By making the simplest assumption possible, namely that Hippuran passes from blood to kidney to urine, the resultant three compartment model appears to adequately explain the shape and time course of the curve.[8] Variants of the radioisotope renogram have been proposed utilizing two additional probes. One is placed over the bladder to follow accumulation of radioactivity in the urine, and the other is positioned over the head in order to follow disappearance of radioactivity from the blood stream. The greatest value of the radioisotope renogram appears to be in the screening of patients, particularly those with hypertension who may have underlying renal disease.[9] The procedure has also gained use in following renal function after pelvic or abdominal irradiation,[10] and in gynecologic patients.[11]

The radioisotope renogram is a simple procedure whose one drawback is the initial expense for the dual counting and recording system required. The procedure is innocuous, and may provide definitive information in a number of patients.

Renal Blood Flow Studies

In certain cases of reduced blood flow to a kidney, corrective surgery can be undertaken (as in constriction of the renal artery). Hence, any studies which can give a quantitative value to the blood flow to the kidneys, are of potentially great use. Sevelius and Johnson[12] reported that counting over the heart and kidneys, following injection of albumin-I^{131} could be used to quantitate renal blood flow. In normal patients their values were: cardiac output 4,518 cc/min., right kidney blood flow 715 cc/min., left kidney blood flow 699 cc/min. This particular technique has not gained wide use because of difficulties in the interpretation of results (data must be read from extrapolated graphic plots which are open to significant human error). In principle at least, this is a possible technique for estimating renal blood flow.

The concept of clearance has proven of use in studies of renal function for many years. $C = \frac{U.V.}{P}$ where the clearance (C) is given in terms of the urinary concentration of the material (U) multiplied by the urine flow per unit time (V in cc/min.), and divided by the plasma concentration of the material (P). C has the units of cc/min., and can be viewed as the volume of plasma cleared of the material under study per unit time. The compound para-amino-hippurate is a fair indicator of renal plasma flow, since it is nearly all cleared upon passing through the kidneys (that is, it passes out via both the glomeruli and tubules). Unfortunately, para-amino-hippurate can not be produced so that it contains a gamma-emitting radioisotope which can be counted externally. Hippuran appears to mimic para-amino-hippurate excretion in some species, and its use has been proposed as an indicator of renal plasma flow.[13,14] Dore and co-workers have discussed an interesting use of Hippuran.[15] They pointed out how, by maintaining a constant blood level of radioactive Hippuran by controlling an infusion, renal plasma flow could be quantitated without urine collection, and the flow into each kidney calculated. Such studies have not yet gained wide clinical use, but they hold promise of usefulness in selected patients.

Glomerular Filtration Rate

It will be recalled that certain materials, such as inulin (a polymer of fructose), pass out from the blood into the urine through glomerular action alone (without addition to or subtraction from the tubules). The removal of such materials from the blood is thus an indication of the glomerular filtration rate (which normally is about one-fifth of the renal plasma flow). Some laboratories are working on the production of inulin-I^{131}. If this compound can be obtained in a form suitable for clinical use, estimation of glomerular filtration rate by external counting will be a good possibility. Until this is achieved, there may be two other methods for estimating glomerular filtration rate through use of gamma-emitting radioisotopes.

a. If tubular secretion of Hippuran is blocked by use of another substance, Hippuran passes out only in the glomerular filtrate. Under such circumstances it can be utilized to estimate the glomerular filtration rate.[16] Other I^{131} labeled dyes have also been proposed for use in determining glomerular filtration.[17]

b. A recent method involves the use of vitamin B_{12} which contains radiolabeled cobalt[18] (there are two cobalt radioisotopes commonly employed; these are listed in Table II, along with the other radioisotopes that have been discussed). After saturation of the patient with stable vitamin B_{12}, Co^{57}-vitamin B_{12} was given intravenously. The vitamin was not handled by the tubules, but appeared to pass out in the glomerular filtrate, and its clearance

Table II

Summary of the Principal Radioisotopes Used in Studies of the Renal Apparatus.

RADIO-ISOTOPE	HALF-LIFE	EMISSIONS	COMMENTS
I^{131}	8.1 days	0.36 MEV* gamma plus other emissions	Used in I^{131}-dyes such as Hippuran
Hg^{203}	46 days	0.28 MEV gamma plus beta	Can be synthesized into Hg^{203}-diuretics
Co^{57}	270 days	0.12, 0.13 MEV gammas plus other emissions	Incorporated into vitamin B_{12}, for evaluation of glomerular filtration rate
Co^{60}	1,930 days	1.17, 1.33 MEV gamma plus beta	

* MEV = million electron volts

closely approximated the glomerular filtration rate. There is thus some possibility of using the procedure in routine clinical studies.

A Resume

The inaccessibility of the kidneys has prompted development of several tests for evaluating their size, location and function. The radioisotope studies often supplement more conventional procedures, and in some cases provide definitive data that cannot be obtained by other methods. The radiation delivered to the patient is on the order of that obtained in the simpler X-ray studies, and the cost is in the range of most other diagnostic procedures.

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Principles Of Medical Sciences

In reviewing the principles of method by which the task of the medical sciences is to be carried forward we have reason to group the resources available into three classes: first, experiment with animals; secondly, experiment with man; and, thirdly, clinical observation. All of these methods are necessary for sound and continuous progress, but each has its special province, and each has certain limitations which prevent its being wholly independent of the others.—*The Collected Papers of Wilfred Trotter,* F.R.S. London, Oxford University Press, 1946, p. 125.

Hemophilus Influenzae Meningitis In An Adult

William F. Eckhardt, Jr., M.D.

Hemophilus influenzae meningitis is an uncommon disease after the age of five years. Dolphin and Popham in 1951 reviewed the world literature from 1899 to 1948 and collected a total of 912 cases of all age groups and found only nine cases in patients between 20 and 30 years of age and only 16 more cases in the age groups over 30 years of age.[1] Merselis and co-workers re-reviewed the literature in 1961 and found a total of 44 cases of influenzae meningitis in patients over the age of 20 years.[2] They added 11 additional cases from their three individual reviews by Hsu-Ming and Tsai-Tao added an additional case in a 67 year old debilitated female, and a summary of the experience from the Mayo Clinic added one more case in the 30 to 50 age group.[3, 4]

It is my purpose to report an additional case of Hemophilus influenzae meningitis in a 54 year old woman.

Case Report

A 54 year old white female was admitted to the Norwalk Hospital in November of 1961 complaining of severe headache and chills. At age eight years, a right radical mastoidectomy was performed for acute mastoiditis. She had occasional bouts of suppurative otitis media during her adolescence but she had remained well except for occasional sinusitis and serous drainage from her right ear. Upon admission to the hospital, she was incoherent, combative and mentally confused. Physical examination was normal except for a stiff neck, photophobia, and serous drainage from her right ear.

Routine laboratory studies were normal except for an elevated white blood count of 20,750 cells/cu. mm. with an increase of young white cell forms. A lumbar puncture showed that her spinal fluid was grossly purulent with a cell count of 2,060 cells/cu. mm., a CSF protein of 432 mgm. per cent, and a spinal fluid sugar of 23 mgm. per cent. Nose and throat and ear cultures showed only the presence of normal flora. Several blood cultures did not grow an organism. Penicillin 1.2 million units intramuscularly every 2 hours, chloramphenicol 6 grams daily, sulfadiazine 6 grams daily and streptomycin 2 grams intramuscularly were begun. On the next day, Hemophilus influenzae B was isolated from the spinal fluid culture. Penicillin was discontinued and sulfadiazine, chloramphenicol and streptomycin were continued. Repeat lumbar puncture four days later showed a decrease in the cell count to 285 cells/cu. mm., a CSF protein of 142 mgm. per cent, and a CSF sugar of 30 mgm. per cent. A chest x-ray was normal. X-rays of the skull showed sclerosing mestoiditis of the right mastoid bone without evidence of cholesteatoma formation. X-ray examination of the para-nasal sinuses showed thickening of the lateral wall of the right maxillary sinus. The left maxillary sinus and sphenoid, ethmoid and frontal sinuses were clear.

Her temperature remained elevated for seven days and then fell gradually to normal. Sulfadiazine and streptomycin were discontinued after seven days and chloramphenicol was continued for the next ten days. Final lumbar puncture on the day before discharge on the 17th day of her illness was normal.

Discussion

The mortality from Hemophilus influenzae meningitis in adults remains high in spite of the fact that the bacteria are always sensitive to most antibiotics and sulfonamides. Four of the 11 patients reported by Merselis and co-workers died. Their age ranged from 31 to 74 years of age. Two of the four patients who died had complicating diabetes mellitus, and a third patient had a complicating ethmoidal sinusitis and cellulitis of the face. Only three of the eleven patients had no underlying complications.[2]

In their review of the Mayo Clinic's experience with 294 patients of all age groups seen from 1948-1958, Eigler and co-workers stressed that underlying disease or injury or prior inadequate antibiotic therapy made recognition of meningitis difficult and delayed effective antibiotic therapy. Early diagnosis and immediate appropriate antibiotic therapy thereby resulted in the highest cure rates.

Prior to antibiotic therapy, the prognosis of influenza meningitis was poor. Although intrathecal medication had a brief trial, most authorities agree that it is no longer indicated. Although chloramphenicol treatment alone may be the most effective treatment of Hemophilus influenzae meningitis, Quaade and Kristensen found no mortality in 36 patients treated with streptomycin and sulfonamides.[5] Adequate results have been obtained with combinations of penicillin and chloramphenicol, streptomycin and sulfonamides, tetracycline and sulfonamides, and streptomycin, sulfonamides, penicillin and tetracycline.

When confronted with the problem of suspected meningitis, it seems logical to begin multiple antibiotic treatment, penicillin, streptomycin, sulfon-

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amide and chloramphenicol while awaiting cultural identification of the offending organism. Since chloramphenicol can rapidly cross the blood-brain barrier, it would seem to be the ideal major antibiotic for treatment of Hemophilus influenzae meningitis in the adult.

Summary

1. The 58th case of Hemophilus influenzae meningitis in an adult is reported in detail.

2. Hemophilus influenzae meningitis in the adult occurs predominently in patients who have chronic ear or sinus infections or who are debilitated from other chronic disease.

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Amyl Nitrate And Angina Pectoris

During the past winter there has been in the clinical wards one case in which the anginal pain was very severe, lasted from an hour to an hour and a half, and recurred every night, generally between two and four A.M.; besides several others in whom the affection, though present, was less frequent and less severe. . . .

When chloroform was given so as to produce partial stupefaction, it relieved the pain for the time; but whenever the senses again became clear, the pain was as bad as before. Small bleedings of three or four ounces, whether by cupping or venesection, were, however, always beneficial; the pain being completely absent for one night after the operation, but generally returning on the second. As I believed the relief produced by the bleeding to be due to the diminution it occasioned in the arterial tension, it occurred to me that a substance which possesses the power of lessening it in such an eminent degree as nitrite of amyl would produce the same effect, and might be repeated as often as necessary without detriment to the patient's health. On application to my friend, Dr. Gamgee, he kindly furnished me with a supply of pure nitrite which he himself had made; and on proceeding to try it in the wards, with the sanction of the visiting physician, Dr. J. Hughes Bennett, my hopes were completely fulfilled. On pouring from five to ten drops of the nitrite on a cloth and giving it to the patient to inhale, the physiological action took place in from thirty to sixty seconds; and simultaneously with the flushing of the face the pain completely disappeared, and generally did not return till its wonted time next night.—T. L. Brunton. "Use of Nitrite of Amyl in Angina Pectoris." *The Lancet,* 2: 97, 1867.

Pulmonary Angiography In Diseases Of The Chest

Julian H. Capps, M.D. and Richard H. Greenspan, M.D.

Introduction

■ For the past quarter of a century the use of angiographic techniques has been directed primarily at studying the cardiovascular system. It is only in recent years that angiography has been applied specifically to the study of the pulmonary vascularity and it has proved of invaluable assistance not only in the diagnosis of various pulmonary conditions, but also in the evaluation of carcinoma of the lung and other pulmonary and mediastinal masses prior to surgical procedures.

In general, there are two major categories of lesions for which pulmonary angiography is especially applicable. First to be considered are the lesions that take their origin from vascular structures, and for which the study may prove diagnostic. In the second category, that of non-vascular lesions, angiography may be done prior to surgery to determine both the vascular supply of a lesion and its proximity to normal vascular structures. It is the purpose of this paper to amplify on these types of lesions from the standpoint of their angiographic appearance.

Technique

We prefer the erect position for studies of the pulmonary vasculature. This permits better visualization of the entire lung field, since the diaphragms tend to be lower in this position. The anteroposterior view is used most commonly, but frequently a biplane study with lateral views may be valuable. Oblique views are often indicated, especially when the lesion is near the left main pulmonary artery. Since this vessel passes almost straight back, the anteroposterior view foreshortens and hence distorts its projected image. Although some authors advocate bilateral simultaneous injections of basilic veins, we find an injection through a large polyethylene catheter inserted into either brachial vein permits the delivery of a sufficient bolus of contrast material to permit opacification of both the pulmonary arterial tree and the left sided structures including the thoracic aorta. Frequently it is advisable to make the injection into either the right atrium or the right ventricle, to avoid the superimposition of contrast material in the superior vena cava and/or the right atrium. Direct injection into the main pulmonary artery or into either right or left pulmonary artery is occasionally indicated. This requires a more extensive procedure, however, as a formal catheterization must be carried out prior to the angiogram. Iodinated contrast material of the diatrizoate family (Hypaque or Renografin 76 per cent) is most commonly used. The dosage varies with the cite of injection and ranges from up to 50 cc.'s in the pulmonary arteries to 100 cc.'s in the veins. Serial films are necessary to insure that the study will be carried through the late aortographic phase; and we routinely determine the duration of filming necessary to achieve this with a Decholin circulation time. Most patients experience a strong urge to cough at the time of maximum pulmonary artery opacification, but with forewarning this can be controlled. The characteristic generalized flushing that occurs during the systemic phase is also transient and rarely causes significant discomfort.

The important phases of the angiogram depend on the purpose for which the study is done and on the technique of the injection. An intravenous injection permits visualization of subclavian and innominate veins and the superior vena cava. This phase frequently yields valuable information, especially in the evaluation of carcinoma of the lung. In the following sequence, the right atrium, right ventricle and pulmonary arteries are seen to opacify as the bolus of contrast material passes through the heart and into the pulmonary circulation. It then becomes possible to evaluate both the central and peripheral pulmonary vessels as to position, configuration and flow. Another very important part of the study is the pulmonary venous phase. In most instances it is possible to trace pulmonary veins into the left atrium, and to determine whether or not all major venous channels are filling normally and are in a normal position. After the contrast material has passed through the left atrium and the left ventricle, there is usually dense opacification of the thoracic aorta and its major branches. Some

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tumors and many vascular abnormalities will opacify in this, the systemic phase of the study (Fig. I).

Lesions That May Be Diagnosed By Pulmonary Angiography

ABSENT PULMONARY ARTERY

Congenital absence or hypoplasia of a main pulmonary artery may present as a very confusing picture on the plain films of the chest.[1] The lung is usually atelectatic but is occasionally of normal volume but with diminished vascular markings. The angiogram in such an instance may be diagnostic, as no pulmonary artery will be seen over the involved lung. The late phases of the study will often show bronchial collateral vessels supplying the lung parenchyma.

PULMONARY EMBOLISM

Now that surgical techniques are becoming available for the emergency treatment of massive pulmonary embolism, angiography will become an increasingly important diagnostic procedure in this condition.[2] The information sought in the angiogram is either a complete obstruction of a major pulmonary vessel, or a filling defect corresponding to an intramural thrombus. Prior knowledge as to location of the thrombus will be extremely valuable to the surgeon, and may permit less extensive exploration.

PERIPHERAL PULMONIC STENOSIS

The plain film findings in this condition are frequently confusing, and there may be marked distortion of the pulmonary vascular pattern. The angiogram, however, will reveal single or multiple areas of stenosis, usually projecting well into the lung field and which show varying degrees of post-stenotic dilatation (Figure II-a).

ARTERIOVENOUS MALFORMATION

This condition is extremely difficult to differentiate from other solitary lesions of the lung, and the characteristic bruit is frequently not heard. The angiogram will show the lesion to be extremely vascular, and the draining veins not only to be large but also to fill earlier than the veins of the remainder of the lung. This is due to the vascular "short circuit" that is present in this lesion (Fig. II-b).

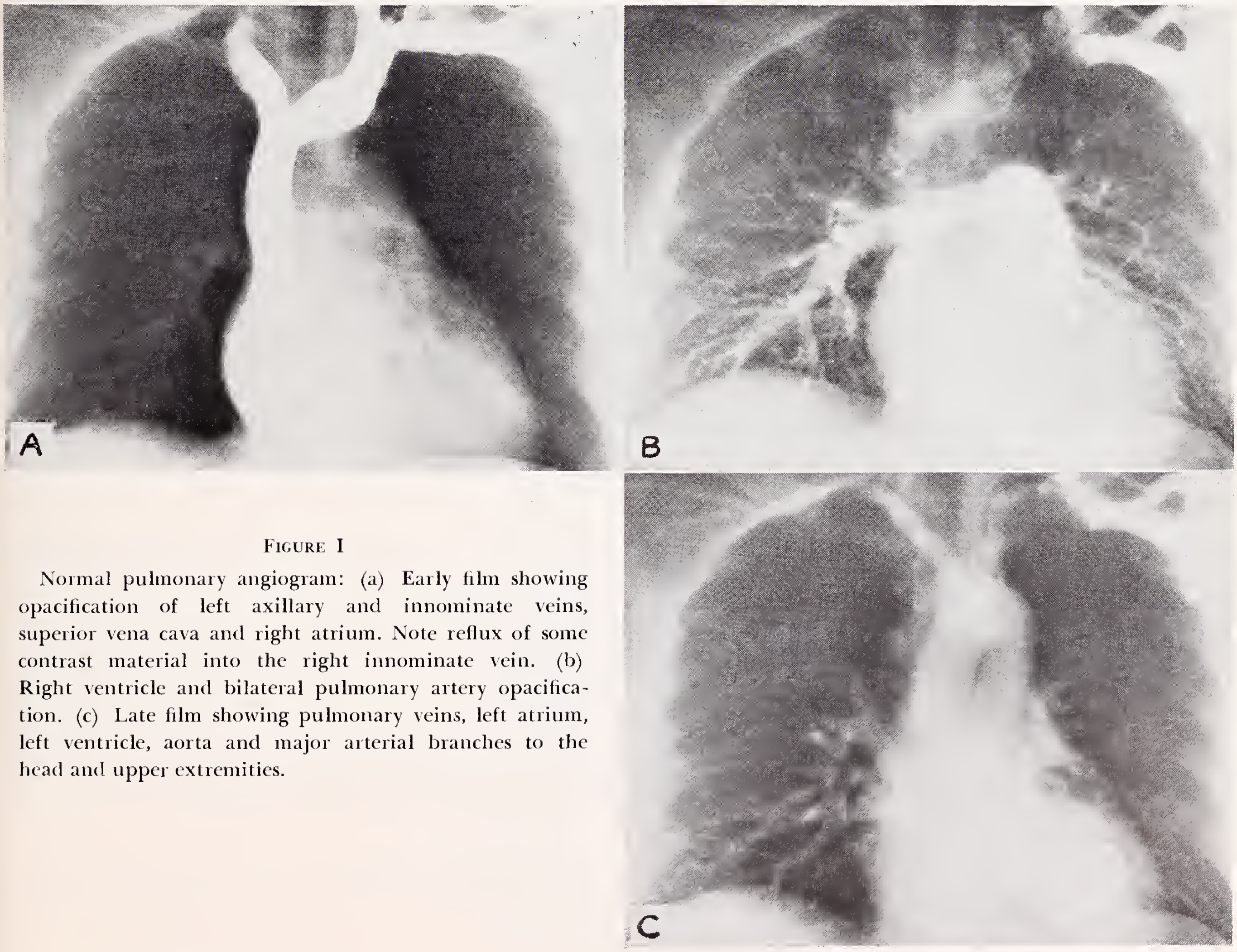

Figure I

Normal pulmonary angiogram: (a) Early film showing opacification of left axillary and innominate veins, superior vena cava and right atrium. Note reflux of some contrast material into the right innominate vein. (b) Right ventricle and bilateral pulmonary artery opacification. (c) Late film showing pulmonary veins, left atrium, left ventricle, aorta and major arterial branches to the head and upper extremities.

ANOMALOUS PULMONARY VENOUS RETURN

Partial anomalous venous return is almost always associated with other congenital defects, especially atrial septal defect. Its diagnosis depends on the demonstration of pulmonary venous return to the systemic venous side of the circulation. Because on the intravenous study there is frequently a persistent minimal opacification of the vena cava and right atrium, and since the diagnosis may depend in part on the opacification of these structures in the late phase of the study, it is desirable to inject the dye either into the right ventricle or the pulmonary

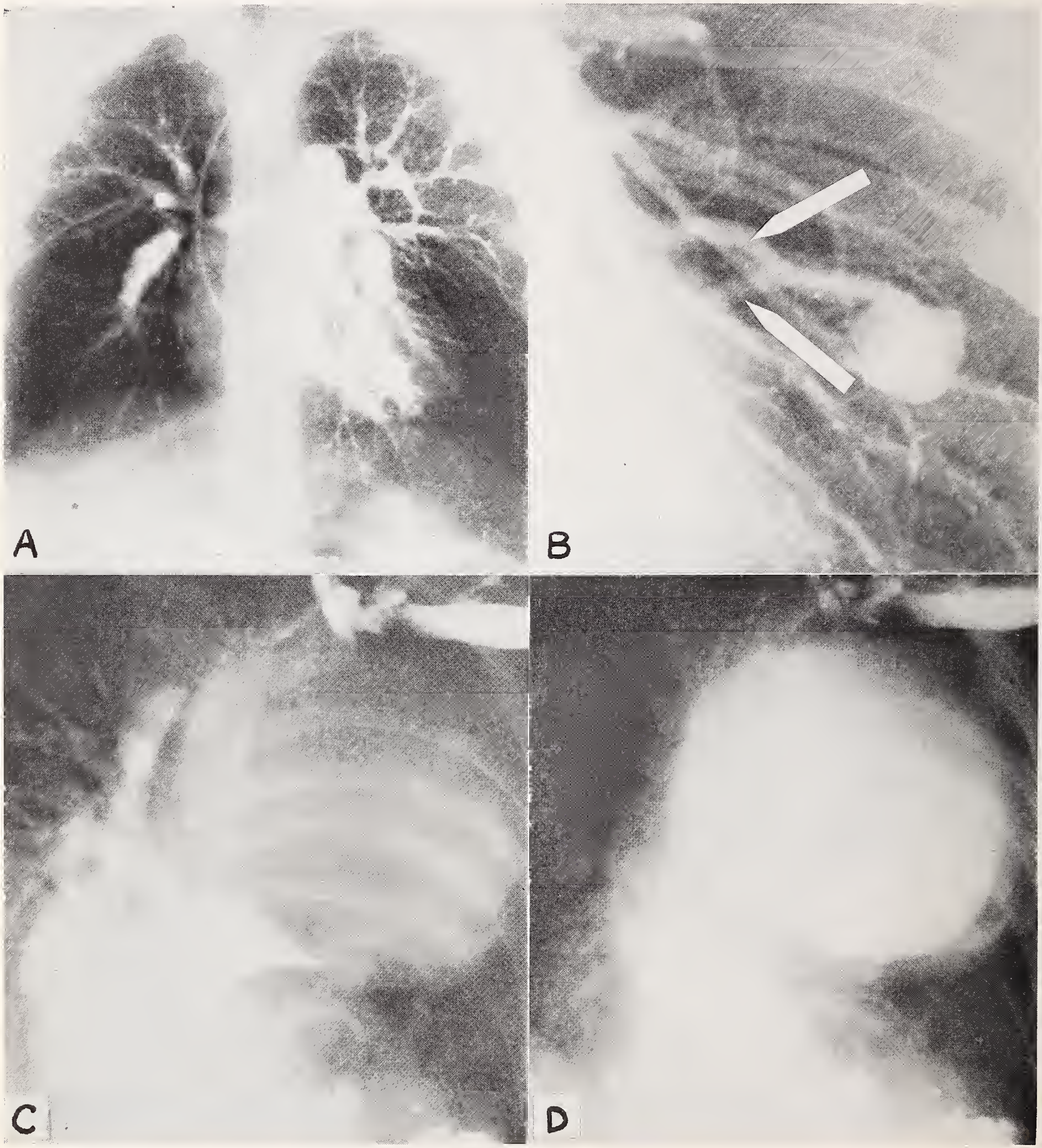

Figure II

(a) Congenital peripheral pulmonic stenosis. Note the multiple areas of narrowing and post-stenotic dilatation bilaterally. (b) Arteriovenous malformation. Top arrow: supplying pulmonary artery. Bottom arrow: draining pulmonary vein. (c & d) Huge traumatic aneurysm of the thoracic aorta, producing stenosis of the left pulmonary artery by extrinsic pressure and opacifying in the aortic phase of the angiogram.

arteries when this condition is suspected.[3] This will permit more valid interpretation of opacification in the right sided structures in the pulmonary venous phase of the study, especially since this may occasionally be the only indication that there is anomalous venous return.

PULMONARY VEIN VARIX

This condition is most often reported in patients with mitral valve disease. It consists of an aneurysmally dilated thin-walled venous sac, and probably is the result of long-standing increased pulmonary venous pressure. It will present as a mass in the lung field, which on angiographic study is seen to opacify only during the venous phase. Its opacification is not early; indeed, it is usually somewhat late and prolonged. Therefore, it is important that serial filming be utilized in the evaluation of this type of lesion.[4]

AORTIC ANEURYSMS SIMULATING A PULMONARY LESION

Aneurysms of the aorta and of the brachiocephalic vessels may present as densities in the lung field or masses in the mediastinum. Occasionally they reach such proportion that pulmonary arteries and veins are displaced or obstructed. The angiogram in such cases will demonstrate the mass to opacify only in the systemic phase of the study, and not only can the diagnosis be made, but also the knowledge of the position of the aneurysm in relation to other vascular structures can be determined (Fig. II-c & d).

BRONCHOPULMONARY SEQUESTRATION

This unusual lesion may present itself in a variety of ways. It may resemble a lung cyst or abscess but is usually seen as a homogeneous mediastinal density. The angiogram will reveal that the vascular supply to the lesion arises from the aorta, with no demonstrable blood supply from the pulmonary arterial tree. Often, however, the vessels are very small and may not be well seen with the forward angiogram. There should be no hesitation, in such a case, to performing a retrograde aortogram, since the presence of systemic vessels supplying the pulmonary lesion may be diagnostic.

OTHER VASCULAR TUMORS

Few other vascular or metastatic tumors of the chest or mediastinum possess sufficient vascularity to become opacified by ordinary angiographic means. We have encountered opacification during the systemic phase of an angiogram in five cases of thyroid tumors, however; three were substernal thyroids, one an ectopic thyroid adenoma in the anterior mediastinum and the fifth a metastatic thyroid carcinoma involving the pelvis. Although this behavior of the tumor cannot be considered diagnostic, a thyroid origin of such lesions should be strongly considered.[5]

LESIONS WHICH MAY BE EVALUATED BY PULMONARY ANGIOGRAPHY

The lesion for which pulmonary angiography is most frequently performed for the purpose of evaluation is carcinoma of the lung.[6,7] Alterations of the pulmonary vascularity in the presence of carcinoma are not characteristic of that lesion, but by demonstrating whether or not major vessels are involved by the tumor one may frequently determine if the lesion is resectable. If the superior vena cava or atrial wall can be shown to be involved, an unnecessary exploratory operation may be prevented (Fig. III-a). The relationship of the tumor to central pulmonary arteries and veins may determine whether or not resection is feasible, since the degree of obstruction or distortion of these structures indicates to the surgeon the extent of mediastinal involvement (Figs. III-b, c, d and e). Abnormalities of lobar or peripheral arteries are not in themselves an indication of inoperability, and it may even be possible to limit resection to a segment or lobe if the involvement is seen to be localized. It is important to remember, however, that all of these changes in the main pulmonary vessels may be produced by lesions other than cancer. Therefore, in interpreting the findings, it is important to have established that the lesion is cancer either by means of scalene node biopsy, bronchoscopic biopsy or sputum cytology. Benign mediastinal tumors, fibrosing mediastinitis, inflammatory and congenital lesions of the hila and lung fields may produce changes on the angiogram identical to those seen with malignant tumors.

Reversal of blood flow in pulmonary artery due to arteriovenous retrograde shunting of blood through hypertrophied bronchial collateral vessels into the pulmonary artery may produce changes simulating a blocked pulmonary artery. When this is seen, it almost invariably is associated with an inflammatory lesion, usually chronic bronchiectasis or pulmonary abscess.[8] This is an extremely difficult condition to interpret, and retrograde aortography may frequently be necessary to visualize the bronchial collateral vessels. In such cases, because the flow is from the high pressure systemic circuit into the relatively low pressure pulmonary artery, the previously non-filled pulmonary artery will opacify.

In bullous emphysema the pulmonary angiogram will reveal displacement of the pulmonary arteries, but no obstruction should be seen at any point. The distortion is due to the presence of large bullae displacing normal lung, with resultant crowding of the vessels. Since patients with this condition are frequently poor candidates for bronchography, because of severely compromised pulmonary function, angiography may be the procedure of choice to outline the involved areas of the lung.

Summary

Pulmonary angiography is a valuable tool in the diagnosis and as a guide to the therapy of certain lesions of the chest. If the lesion is primarily a vascular one, the angiogram may be diagnostic. Non-vascular lesions may be evaluated by pulmonary angiography as to their relationship to major vascular structures. Such information may be used to determine whether or not a carcinoma is resectable. The techniques are simple and safe and flexible enough that the examination can be individualized to suit the particular patient being studied.

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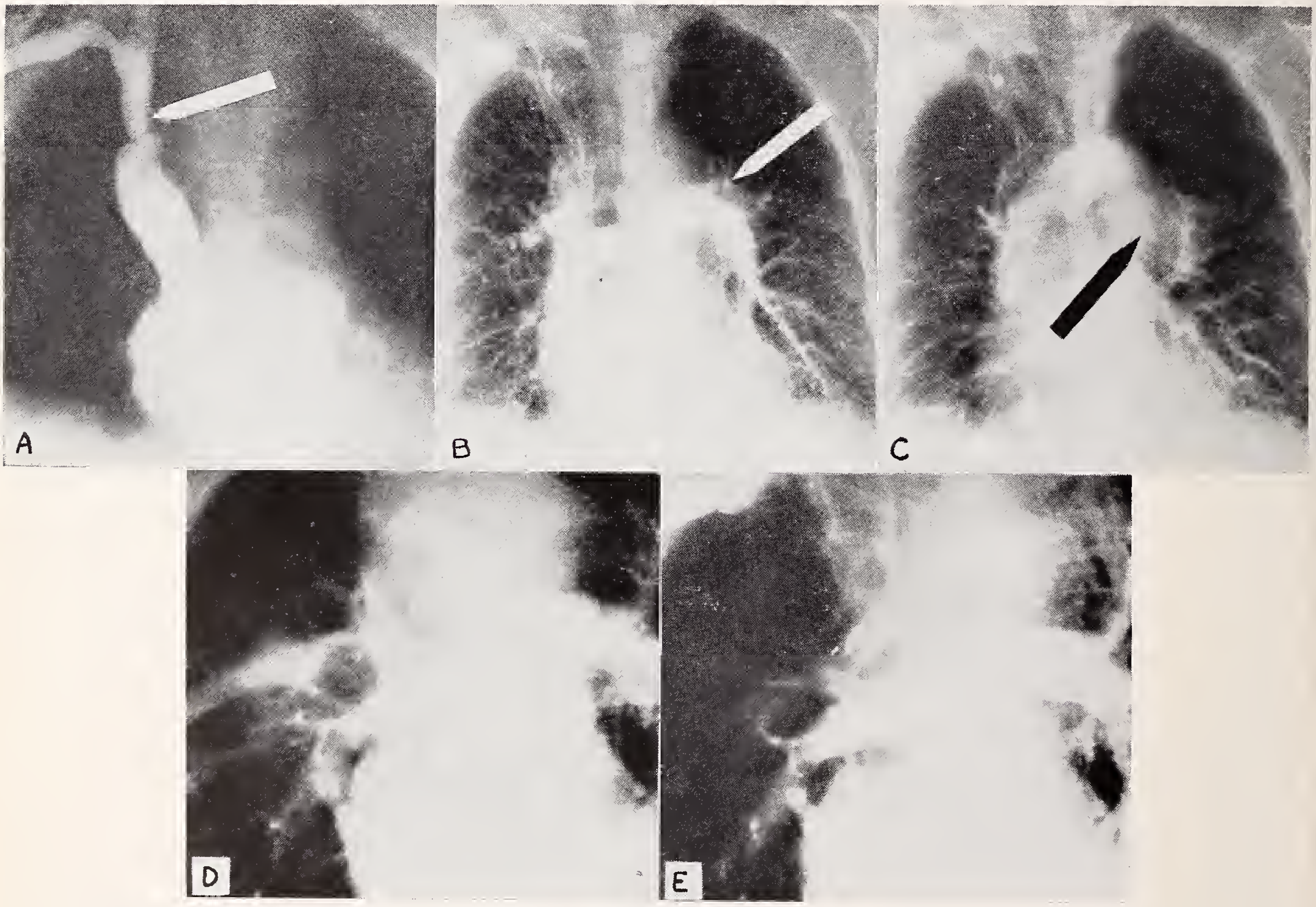

Figure III

(a) Carcinoma of the right lung with mediastinal metastasis. The defect at the junction of the right innominate vein and superior vena cava represents tumor invasion of these structures. This lesion was unresectable. (b & c) Diminished arterial flow to the left upper lobe in a patient with carcinoma of the lung and hilar invasion. Note also the poor filling of the superior pulmonary vein on the left, another sign of diminished arterial flow. (d) Carcinoma of the right lung with hilar metastasis producing spreading at the junction of the truncus anterior and lower lobe pulmonary arteries. (e) Same patient following a complete course of radiation therapy showing a decrease in size of the mass.

Social Class And Mental Illness: A Ten Year Follow-up Of Psychiatric Patients

Jerome K. Myers, Ph.D., Lee L. Bean, Ph.D., and Max P. Pepper, M.D.

■ This is the first report on a ten year follow-up study of persons enumerated in the psychiatric treatment census taken in the New Haven community in 1950.[1] In the original study, significant relationships were discovered between social class and the prevalence, treatment, and development of diagnosed mental illness.[2] The present study focuses upon relationships between social class and what has happened to the patients in the ten years following the original study. Specifically, significant relationships were hypothesized between social class and 1. the patients' current treatment status (discharged from treatment, dead, or still in treatment), 2. relapse rates of patients discharged from treatment, and 3. the current mental status and social adjustment of patients discharged from treatment and living in the community.[3]

Research on the experiences of psychiatric patients after treatment has increased in recent years. Follow-up studies have investigated such problems as the effectiveness of different therapies and treatment agencies for the various disorders, the readjustment of former patients in the community, social and psychiatric factors related to release and relapse, and the mental status and social adjustment of former patients after they have become settled in their home communities. Generally, such studies have focused upon a specific problem relating to the former mental patient and thus have limited their scope. Most careful follow-up studies, for example, include only a small number of cases, patients from one treatment agency, persons of one sex or a single psychiatric diagnosis, or some other relatively homogeneous group of patients. Moreover, most investigators have restudied their subjects at relatively short periods after discharge from treatment or after the original study—a few months to a few years at most.[4]

The present research differs from most previous investigations in being more comprehensive and covering a longer follow-up period. It attempts to determine what happens to a large number of patients under specified conditions from a variety of treatment agencies over a ten year period. It is also the first follow-up study to focus upon social class. The findings reported in this article deal with a single aspect of the research, namely, the relationship between social class and the 1960 treatment status for patients who were in hospital care in 1950.

Methodological Procedures

The status of all individuals in greater New Haven, 1,565 in number, who were in psychiatric treatment between May 31 and December 1, 1950 in psychiatric out-patient clinics or psychiatric hospitals, was re-examined on June 1, 1960.[5] Patients treated by private practitioners in 1950 were not restudied because of commitments the research group made to these physicians at the time of the original psychiatric census.

The research consisted of two phases: 1. a study of records of the 1950 and subsequent treatment agencies, and 2. interviews with patients discharged from treatment and living in the community as of a given cut-off date (June 1, 1960) and their families, to determine their mental status and social adjustment in the community. A matched control group of persons who were never patients was also interviewed for the second phase of the research.

In the first phase, a 43 item schedule was used to abstract social, psychiatric and medical data from hospital and clinical records covering the patients' histories during the ten years studied. Materials collected for patients who are still in hospital treatment or who died in treatment were limited to this schedule. In the second phase, extensive additional information was gathered through interviews for those persons studied.

The independent variable, social class, was measured by Hollingshead's Two Factor Index of Social Position.[6] Rating scores on occupation and education, appropriately weighted and combined, group themselves into five clusters or social classes. A brief descriptive characterization of these social classes follows: *Class I* (the highest socio-economic

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position) comprises families of wealth, high education and occupation, and top rank social prestige. *Class II* consists of families in which the adults, for the most part, hold college or advanced degrees, and are in professional or high level managerial positions. *Class III* includes the bulk of small business and white collar workers, together with a sizeable number of skilled workers. This group consists predominantly of high school graduates. *Class IV* consists largely of semi-skilled workers with some secondary education. *Class V* includes unskilled and semi-skilled workers who have an elementary education or less.

Selected Findings

This paper presents selected findings relevant to the hypothesis that there is a significant relationship between social class and the patients' follow-up treatment status.[7] All cases in hospital treatment in 1950 are included in this analysis. Persons who were in out-patient care at that time will be treated in further reports. At the time of the original study there were 1,420 patients in state, private and veterans hospitals. Of this number, 53 per cent were still hospitalized in 1960, 31 per cent had died, 13 per cent were no longer hospitalized or under any psychiatric treatment, two per cent were discharged from the hospital but under out-patient care, and less than one per cent (eight persons) could not be located.

The data in Table I demonstrate a strong relationship between social class and follow-up treatment status. Significantly more persons in the lower classes were still hospitalized ten years after the original 1950 study. Whereas 38 per cent of Class I and II individuals were in hospitals in 1960, the percentage increased steadily to 48 in Class III, 52 in Class IV and 56 in Class V.[8] The percentage of persons who had died differed neither greatly nor in any consistent manner among the classes. However, the percentage living in the community and no longer hospitalized declined steadily from 30 in Classes I and II, to 27 in Class III, 18 in Class IV, and 10 in Class V. Thus the proportion of persons discharged from hospital treatment in the two highest classes was three times as great as in the lowest class. Most persons discharged from the hospital were no longer under any type of psychiatric care. However, those receiving out-patient care were concentrated in the middle and upper classes. Whereas only one per cent of former Class V patients were being treated in a clinic or by a private practitioner, the percentage rose to nine in Classes I and II.

TABLE I

1960 TREATMENT STATUS BY SOCIAL CLASS OF HOSPITALIZED PATIENTS

1960 TREATMENT STATUS	SOCIAL CLASS I-II	III	IV	V	TOTAL
	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Hospitalized	38	48	52	56	53
Dead	30	24	30	33	31
Discharged from Hospital:	30	27	18	10	15
a. Not under treatment*	(21)	(23)	(16)	(9)	(13)
b. Out-patient treatment*	(9)	(4)	(2)	(1)	(2)
Unknown**	2	1	—	1	1
	100%	100%	100%	100%	100%
N =	47	122	560	691	1420

$\chi^2 = 39.64$ $P < .001$, 6 d f

* Subcategory of "Discharged from Hospital."

** The Unknown cases were not included in the calculation of χ^2.

The percentages in Table I are based upon the total cohort of 1950 hospitalized patients, and thus include persons who had died by 1960 as well as those still alive. If only those persons still living in 1960 are considered, the same class differential is found. The percentage of patients no longer in hospital declined from 44 in Classes I and II, to 34 in Class III, 26 in Class IV, and 15 in Class V.

Since factors other than social class might be related to discharge from treatment, the data were analyzed further. One such factor, length of hospitalization prior to 1950, was related clearly to 1960 treatment status. (See Tables II and III). Only six per cent of persons hospitalized in 1948 or earlier were out of hospital in 1960, while 39 per cent of those individuals hospitalized in 1949 or 1950 had been discharged.

However, the length of hospitalization at the time of the original psychiatric census did not

TABLE II

1960 TREATMENT STATUS BY SOCIAL CLASS OF PATIENTS HOSPITALIZED IN 1949 OR 1950

1960 TREATMENT STATUS	SOCIAL CLASS I-II*	III*	IV	V	TOTAL
	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Hospitalized	15	25	27	32	28
Dead	31	22	31	36	32
Discharged from Hospital	50	53	41	31	39
Unknown**	4	—	1	1	1
	100%	100%	100%	100%	100%
N =	26	45	169	150	390

$^2\chi = 10.02$ $P < .05$, 4 d f

* Classes I-II and III were combined, because of the small number of cases in Classes I-II, in the calculation of χ^2.

** The Unknown cases were not included in the calculation of χ^2.

TABLE III

1960 TREATMENT STATUS BY SOCIAL CLASS OF PATIENTS HOSPITALIZED BEFORE 1949

1960 TREATMENT STATUS	SOCIAL CLASS I-III* PER CENT	IV PER CENT	V PER CENT	TOTAL PER CENT
Hospitalized	63	62	63	63
Dead	26	30	32	30
Discharged from Hospital	10	8	4	6
Unknown**	1	—	1	1
	100%	100%	100%	100%
N =	98	391	541	1030

$\chi^2 = 9.53$ $P < .05$, 4 d f

* Classes I, II and III were combined, because of the small number of cases discharged from the hospital, in the calculation of χ^2.

** The Unknown cases were not included in the calculation of χ^2.

account for the class differences mentioned earlier. As shown in Tables II and III, the same relationship between class and current therapy status existed when length of hospitalization at the time of the original study was controlled. Table II presents data for persons hospitalized in 1949 or 1950, and shows proportionally twice as many Class V as Class I and II patients still in hospital ten years after the original study. Specifically, the percentage still hospitalized increased from 15 in the highest classes to 32 in the lowest. At the same time, the percentage no longer in hospital declined from 50 in Classes I and II to 31 in Class V. If only those persons still living in 1960 are included, the percentage of persons no longer in hospital treatment was 76 in Classes I and II, 69 in Class III, 60 in Class IV, and only 49 in Class V.

Although few persons who entered hospitals prior to 1949 had been discharged by 1960, the number who had was significantly greater in the higher classes. (See Table III). Ten per cent in Classes I—III were no longer hospitalized, compared with 8 per cent in Class IV and 4 per cent in Class V.[9] Again, if those individuals who died are excluded, the same class pattern is found: the percentage of persons no longer hospitalized decreased from 14 in Classes I, II and III, to 12 in Class IV and 7 in Class V.

Further internal analyses of the data established even more strongly that social class was an important determinant of current treatment status. Cross controls were applied for variables presumably related to therapy outcome such as sex, religion, marital status, age, diagnosis, psychiatric treatment experience, major type of treatment, and type of hospital.[10] Four separate analyses were made for these cross-controls. First, a determination of any differences in current treatment status by any of these variables was made. Second, the data concerning only those persons still living in 1960 were analyzed. Next, to control for date of hospitalization, which has been shown already to be related to therapy outcome, a separate analysis was conducted for patients who entered treatment in 1949 or 1950. Finally, a separate analysis was also made for those who entered the hospital prior to 1949.

Two factors—sex and religion—were unrelated to current therapy status in any way when the above four analyses were made. The other six variables were related to treatment outcome in the following manner for each of the four analyses:

1. *Marital status*—The proportion of patients no longer hospitalized in 1960 was greater for the married than for the unmarried, separated, divorced or widowed.
2. *Age*—As would be expected, more persons age 60 and over than below 60 had died by 1960, and fewer had been discharged from the hospital.
3. *Diagnosis* — Significantly more neurotics than psychotics were out of hospital in 1960. Within the psychotic group, the lowest discharge rate was found among the senile psychoses, followed in order by schizophrenic and paranoid psychoses, and all others.[11]
4. *Previous psychiatric treatment history*—Persons who were in their first course of psychiatric treatment at the time of the original study were more likely to have died by 1960 than individuals with previous treatment records.
5. *Major form of treatment* — The highest percentage of patients still hospitalized and the lowest percentage discharged and living in the community were found among those receiving custodial care only in 1950, followed in descending order by patients originally designated as receiving organic treatment, and those receiving psychotherapy.
6. *Type hospital by sponsorship* — The highest percentage of patients no longer in hospital care was found among those originally in private hospitals, followed in order by those in veterans hospitals and state hospitals.

In summary of the above, four separate analyses were made for each of six controls. Twenty-four chi square tests were made to determine whether significant differences existed between 1960 treatment status and the individual factor being controlled. Differences were found at the following levels of significance: in 22 cases, p was less than .01; in one case, p was less than .05; and in one case, p was less than .20.

After determining that these factors were indeed related to 1960 treatment status, the next step was to determine whether any of them accounted for the significant social class differences in outcome already noted. Therefore, detailed analyses were made to determine relationships between social class and 1960 treatment status within each of the specific groupings into which the six controls had been divided. These seventeen specific breakdowns were:

1. *Marital status*—(a) married, (b) single, (c) separated, widowed and divorced.
2. Age—(a) 60 and above, (b) below 60.
3. *Diagnosis*—(a) neuroses, (b) schizophrenic and paranoid psychoses, (c) senile psychoses, (d) other psychoses.
4. *Previous psychiatric treatment experience*—(a) no psychiatric treatment previous to 1950 course of treatment, (b) previous psychiatric treatment.
5. *Major type of treatment*—(a) custodial care, (b) psychotherapy, (c) organic therapy.
6. *Type hospital by sponsorship* — (a) private, (b) veterans administration, (c) state.

Generally, the introduction of these controls did not negate any of the class differences found for 1960 treatment status. In nearly all cases, one discovered the same relationship within each grouping: the higher the social class, the greater the percentage of patients discharged from hospital care. The four separate analyses described above for cross-controls were made for each of the seventeen individual categories, and a chi square test for significance was applied to each of these. In 64 of these 68 tests, social class differences were clear cut. The distribution of significance levels found was: p less than .01—21 tests; p less than .05—23 tests; p less than .10—6 tests; p less than .20—14 tests. In only four cases were the class differences so slight that statistical significance was not even approached. In these, p was greater than .20. The following categories comprise these exceptions:

1. Single patients hospitalized during 1949 or 1950.
2. Persons receiving custodial care, if the dead are excluded.
3. "Other psychotics" hospitalized before 1949.
4. Seniles hospitalized in 1949 or 1950.

Discussion

Since this article limits its consideration to persons who were under hospital care at the time of the 1950 census, these patients were probably more seriously ill and had a poorer prognosis than those being treated in out-patient clinics at that time. Nevertheless, the small percentage no longer hospitalized in 1960 (15 per cent) may be surprising to many readers who are familiar with hospital discharge rates which are higher. This percentage, however, is consistent with the findings of other long term studies which show that considerably more persons are discharged from hospitals than are able to readjust successfully in the community and remain out of treatment.

The element of chronicity in treated psychiatric illness also helps account for the small number of persons living in the community. Since the 1950 treatment prevalence census included all patients then hospitalized regardless of when their treatment began, no differentiation is made between chronic and acute cases in our overall statistics. If only patients hospitalized for less than two years in 1950 are considered, treatment outcome in 1960 was more favorable. As shown in Table II, 39 per cent of such individuals had been discharged from the hospital and were living in the community in 1960. Perhaps more significant, we find that of the 262 persons hospitalized in 1949 or 1950 and still living in 1960, 153 or 58 per cent, were no longer under hospital care.

In contrast, the prognosis for those patients who stay in the hospital two years or longer was poor. Only nine per cent of the 714 individuals living in 1960 who had been hospitalized prior to 1949 had been discharged from hospital care. This low discharge rate for long term patients is not surprising in the light of the social breakdown known to occur in chronically institutionalized patients.

The relationships between our control variables and patients' 1960 treatment status were generally consistent with the results of previous research. That neither the patients' sex nor religion was related to treatment outcome may seem surprising. Previous studies report contradictory findings regarding sex as related to outcome; in surveying the literature no substantial body of research exists which relates religion to outcome. Our results corroborate the findings of many other studies regarding the relationships between treatment outcome and the other control variables: marital status, age, psychiatric diagnosis, previous psychiatric treatment, type of treatment, and type hospital.

Turning to our major interest, the relationship between social class and 1960 treatment status, we found that after ten years the same kind of class differences existed as were found in 1950. Our data show that the higher the social class of patients, the greater was the proportion no longer under hospital care in 1960. That this relationship between social class and follow-up treatment status held for 64 of the 68 tests for control factors is very significant. Even in the four exceptions, the same class pattern obtained, although at a very low level of statistical significance. Since 68 control tests were made, three or four exceptions might be expected on a chance basis alone. Three of the four exceptions pertained to a select portion of the study group: those long hospitalized or older patients with a short life expectancy. Few persons in these groupings had been discharged from hospital treatment by 1960, (i.e. exceptions 2, 3 and 4 noted earlier). Further analysis of our data may clarify further the reasons for the lack of strong statistical significance in these three exceptions, as well as in the fourth: single patients hospitalized in 1949 or 1950.

The next step in our research will be an attempt to determine the reasons for the striking social class differences found relating to follow-up treatment status. Preliminary work indicates that they are probably multiple. Earlier research has demonstrated class differences in the therapy process itself and in treatment experiences among patients. How are such differences related to therapy outcome? Does the willingness and ability of families to have their members return from a psychiatric hospital vary by class? Do community attitudes toward former patients and their incorporation back into the community differ depending upon their social class? Were lower class patients more seriously ill in 1950 than higher status individuals? Answers to such questions, which will help explain the relationships reported in this paper, will be sought from the interview materials collected in the second phase of our research.

Summary

This article reports on a ten year follow-up study of persons enumerated in the Psychiatric Treatment Census taken in the New Haven community in 1950. Data were presented concerning those 1,420 individuals who were hospital patients in 1950. The findings supported the hypothesis that there is a significant relationship between social class and patients' treatment status at follow-up in 1960. As the social class of patients became higher, the proportion no longer hospitalized increased. Reasons for this relationship will be explored in future publications.

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1. This research is supported by USPHS, NIMH Grant MH-03569. The authors are from the Departments of Sociology and Psychiatry of Yale University.

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5. The towns included in greater New Haven are as follows: New Haven, West Haven, East Haven, North Haven, Hamden, and Woodbridge, Connecticut.

6. See August B. Hollingshead, *Two Factor Index of Social Position*, mimeographed publication, copyright, 1957; and Myers and Roberts, *op. cit.*, 130.

7. The chi-square test was used in all computations to determine whether significant differences existed between frequency distributions.

8. Classes I and II are combined in this report because of the small number of cases in Class I.

9. Classes I, II, and III are combined in this analysis because of the small number of cases discharged from the hospital.

10. Patients are classified according to their 1950 status on each of these variables. See Hollingshead and Redlich, *op.* cit., 28-29 and 253-57 for a description of the diagnostic scheme employed and the classification of types of psychiatric treatment and treatment facilities.

11. Because of the relatively small numbers involved, affective and organic psychoses were combined.

A "Plug Catheter" For Percutaneous Retrograde Aortography

Howard J. Ricketts, M.D.

■ Percutaneous arterial and venous catheterization as originally described by Seldinger[1] is now a widely used clinical technique for performing angiographic and catheterization studies. The method is simple, reliable, and permits the introduction of sufficiently large bore catheters to deliver an adequate bolus of contrast medium for angiographic examinations. Inherent in the method, however, is the use of an end-hole catheter, with or without additional side holes. Power injection through such a catheter frequently presents one or more of the following disadvantages: (1) recoil of the catheter tip sufficient to impair the diagnostic quality of the examination; (2) subintimal or subendocardial injection of the contrast medium; (3) a prominent jet of contrast medium that may extend 5-10 cm. beyond the catheter tip, even during retrograde injection in the aorta. This jet is particularly undesirable during retrograde abdominal aortography for visualization of the renal arteries, since it frequently opacifies the branches of the celiac and superior mesenteric arteries which may overlie and obscure the renal vessels.

A closed-end catheter with side holes would obviate most of these disadvantages and, indeed, is frequently used when arterial cannulation is performed surgically. It is the purpose of this paper to describe a modification of the percutaneous catheterization technique which converts the open-end catheter into a closed-end catheter for angiography.

Methods

In order to simulate a closed-end catheter and retain the advantages of the percutaneous technique a metallic "plug" was devised that is firmly fitted to a fine (.016") spring steel wire and inserted into the catheter so as to completely occlude the tip (Fig. I). The plug is turned from stainless steel and is tapered so that it completely fills the catheter tip, thus obliterating any dead space in which a thrombus might form. At the proximal end of the catheter the wire passes through a Seldinger stopcock and a Toughy-Borst male adapter (B-D 611A) specially drilled and fitted with a side-arm made from a three-way stopcock. The rubber gasket in the adapter can be easily tightened around the small wire with sufficient pressure to seal the system, even during pressure injections through the stopcock. This device is also used to seal heparinized saline in the system when the Seldinger guide wire is being used for positioning the catheter. Utilization of the side-arm for injection allows the use of any length catheter with the same metallic tip, as the excess wire extends proximally through the adapter. PE 260 polyethylene catheters have been used in this study, but the metallic tips can be made for any size catheter.

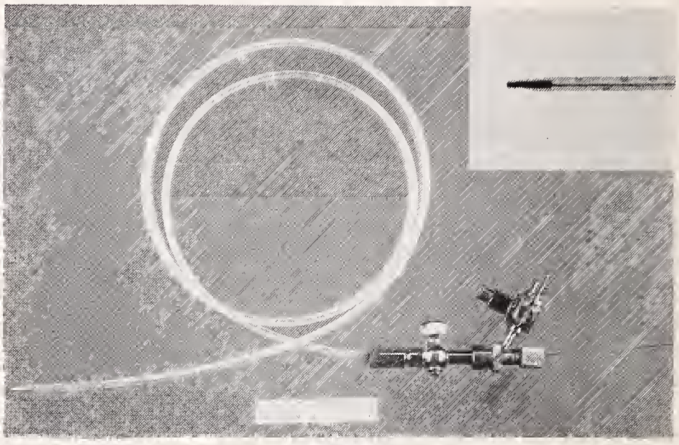

FIGURE I

"Plug Catheter" used for percutaneous aortography. PE 260 polyethylene catheter with Seldinger stopcock and Toughy-Borst adapter fitted with side-arm. Rubber gasket in adapter seals system for pressure injection through side-arm. Inset shows detail of catheter tip with plug in place.

Initially there was some concern that the plug could be dislodged from the spring wire or through the catheter tip. To insure against the former event the wire is hooked within the metallic tip so that the silver solder only functions to stabilize the joint. The tapering of both the metallic plug and the inside diameter of the catheter tip has made it impossible to force the plug mechanically through the tip or to inject it through with as many as 20 consecutive high pressure injections of 90 per cent Hypaque at 8-10 kg/sq. cm.

In Vitro Injection Characteristics

In order to avoid the variables encountered in a pulsatile system, the catheter was first tested in a virtually pulseless model consisting of a sigmomotor pump circulating water through a ¾" (i.d.)

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rubber tube at a flow rate of 4½ liters per minute at a mean pressure of 13 mm. Hg. Multiple cineangiographic and serialographic studies were performed using an Amplatz injector with volumes of 20-60 cc and pressures of 60 to 210 pounds per square inch (p.s.i.). A significant reduction in the retrograde reflux of the bolus occurred when the catheter tip was occluded. The difference was greatest at low injection pressure (less than 100 p.s.i.). The degree of reflux was independent of the volume injected. The prolonged, constant opacification of a segment of "aorta" is well demonstrated in Figure II and led to the use of lower injection pressures in experimental and clinical subjects. The cine studies showed a marked difference in the appearance of the wave front of the bolus. Using a catheter with an open-end tip and side-holes the wave front was convex upward during retrograde injections. With the closed-end catheter the wave front was concave upward, the major portion of the bolus being injected toward the periphery of the vessel lumen. The latter is certainly more desirable for opacification of branches of the aorta.

Factors affecting the injection time were studied during multiple timed injections into a glass container. Timing was done with a stopwatch and was reproducible within 0.2 seconds. Fifty cc. of 76 per cent Renografin were injected through a 75 cm. PE 260 polyethylene catheter with 5 side holes at a pressure of 150 p.s.i. This pressure was selected on the basis of the studies in the model system and on an estimate of what would be needed clinically. The results show that the presence of the fine wire and its tip increased the injection time by an average of 25 per cent with the catheter tip occluded (3.1 sec.) compared with injection through the open tip (2.5 sec.). Injections in both instances were made through the side-arm stopcock, a factor which added about 10 per cent to the injection time compared with injection directly into the end of the catheter. Thus the injection time, at this pressure, is prolonged about one-third compared

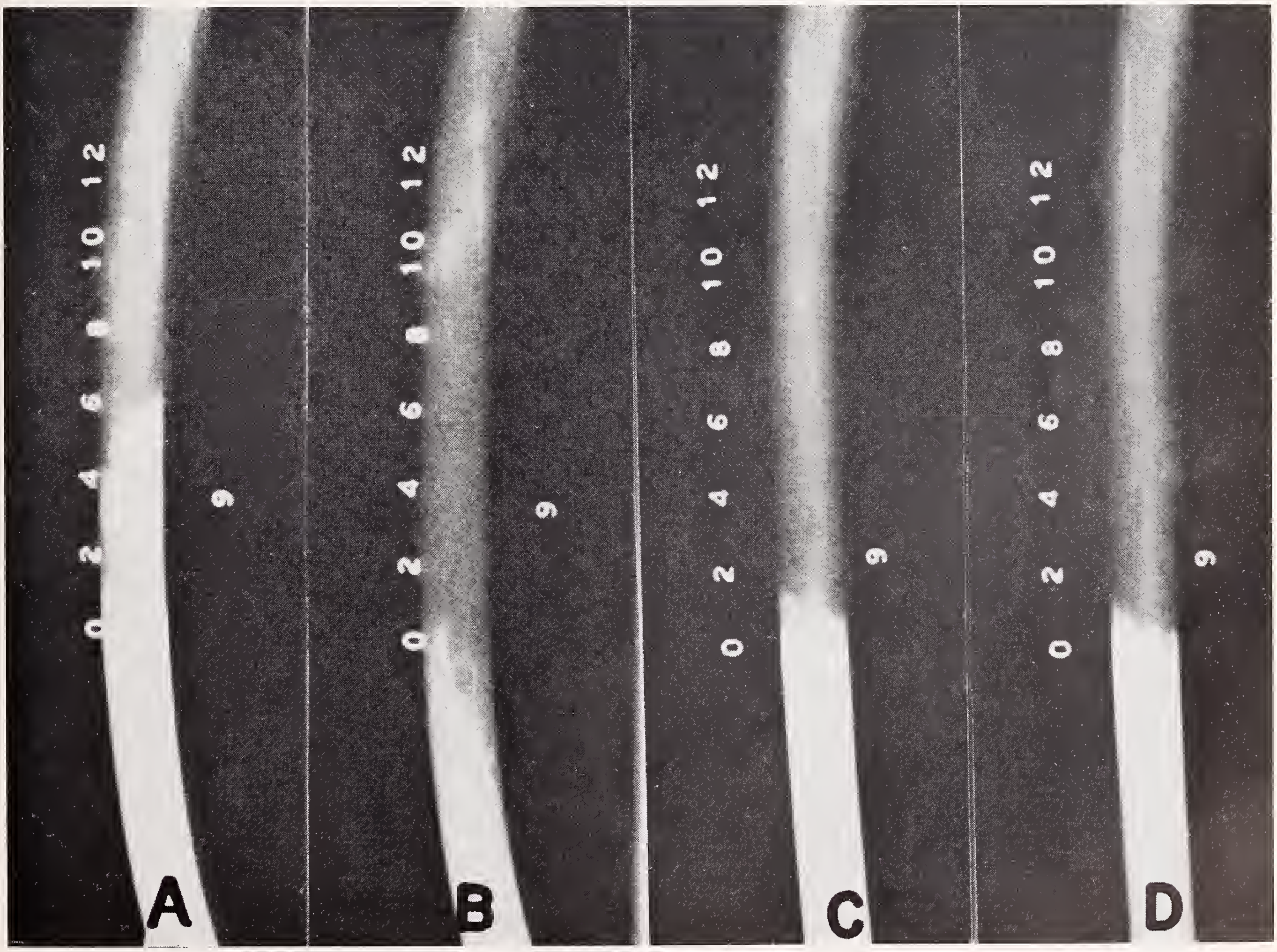


FIGURE II

Retrograde injection in model system with essentially pulseless flow. (Direction of flow is from top to bottom of illustration). Centimeter scale on left with catheter tip at O. 20 cc. of Renografin, 76 per cent, injected at 120 p.s.i. Films exposed at 6 per second. A. Injection with catheter tip open. B. ⅔ of a second later. C. Injection with tip occluded by metallic plug. D. ⅔ of a second later.

with injection directly into a similar but open-end, catheter.

All side-holes were made with a punch producing a hole 1.2 mm. in diameter, or about one-third the area of the catheter lumen. Multiple timed injections showed no significant decrease in the injection time when more than three side holes were used. More side-holes offered better distribution of the bolus without appreciable gain in the rapidity of the injection.

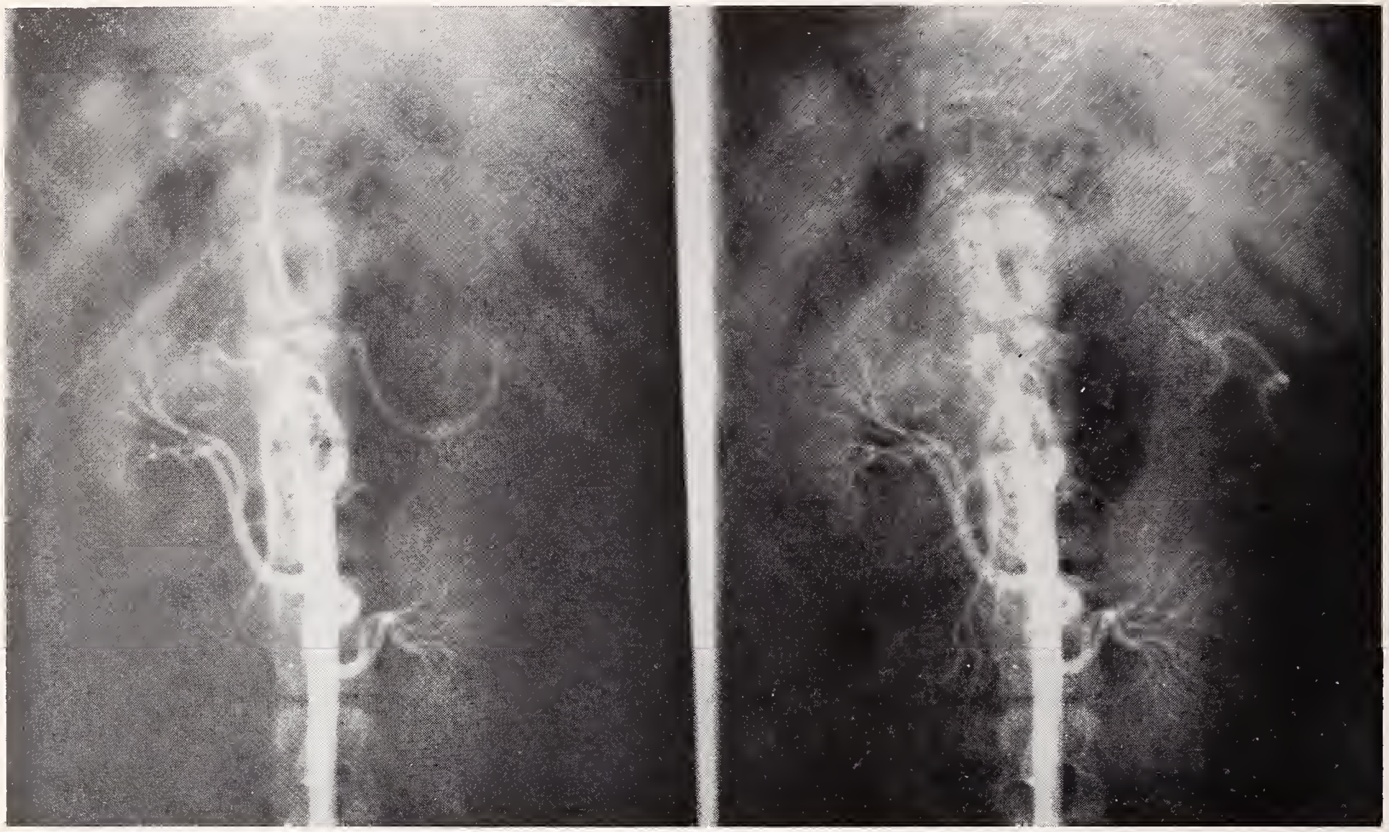
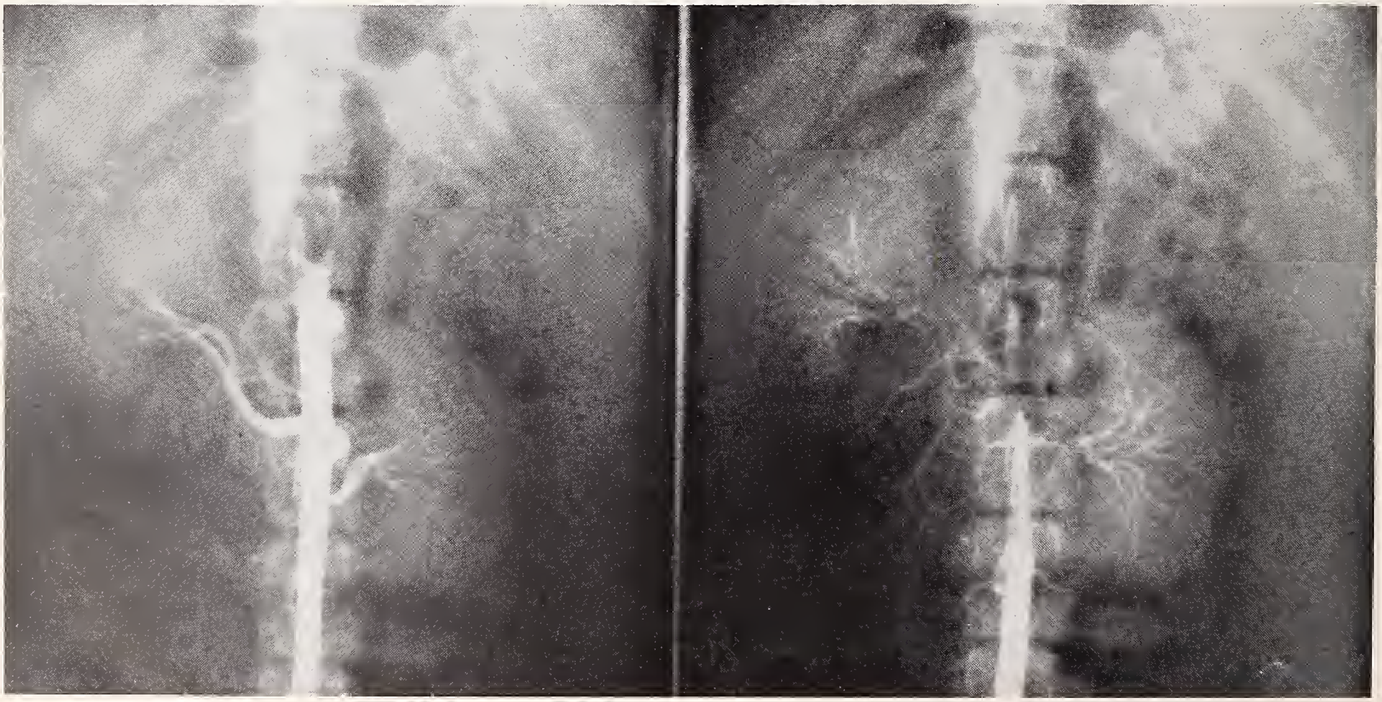


Figure III

Retrograde aortogram in a 32 kilogram dog using 15 cc. of 60 per cent Renografin injected with 120 p.s.i. Films obtained at 6 per second and selected to show maximum reflux during each injection. (Above) Injection with catheter tip open and next film 1/6 second later. Notice the opacification of the celiac and superior mesenteric vessels on both films. (Below) Identical injection, but with "plug" in place. Films 1/6th of a second apart. Notice the reduced intensity and duration of reflux and the delayed and diminished opacification of the superior mesenteric and celiac arteries.



In Vivo Experimental Studies

Retrograde aortography in dogs demonstrated a distinct decrease in opacification of the celiac and superior mesenteric arteries when the metallic plug was used (Fig. III). The localization of the bolus was not as dramatic or as consistent in a pulsating blood stream as it was in the constant flow model. In the animals the extent of aortic reflux with the catheter tip occluded often appeared similar to that seen during injection with the tip open. The significant difference, however, was the reduction in density and duration of the refluxed bolus and the resulting reduction in opacification of the aortic branches proximal to the renal arteries.

Clinical Results

At the time of writing 24 clinical percutaneous retrograde aortograms for renal artery visualization have been performed using the "plug catheter." Although comparative studies have not been made on the same patient, there appears to be considerable improvement in the visualization of the renal vessels compared with similar studies using an open-end, side-hole catheter (Fig. IV). Reflux of the bolus often extends 5-8 cm. above the catheter; but as demonstrated experimentally, the intensity and duration of the refluxed bolus is considerably reduced.

The retrograde study is prolonged by only a few seconds. The catheter is positioned in the usual manner. The spring guide is then removed, and the metallic plug and wire are inserted through the adapter and firmly pressed into the catheter tip. Final positioning is done under fluoroscopic control with the plug in place. Correct positioning of the catheter is critical if opacification of overlying vessels is to be minimized. The plug should appear at the superior portion of the second lumbar vertebral body, leaving the side-holes opposite, or slightly distal to, the orifices of the renal vessels. A volume of 25-30 cc. of 75 per cent Hypaque, or 76 per cent Renografin, is usually injected with an Amplatz injector at a pressure of 115-150 p.s.i. A 75 cm. PE 260 polyethylene catheter with 4 side holes is used. The same plug also has been used with size 8 Teflon catheters.

Further localization of the injected bolus may be possible by timing the injection with the cardiac cycle in a manner similar to that recently reported by Voudoukis and Boucek.[3] Supravalvular injections are much more satisfactorily performed with closed-end catheters and represent another area where it is hoped this modification of the percutaneous technique will be useful.

Summary

A modification of the Seldinger technique for percutaneous retrograde aortography is described. A metallic "plug" on a fine spring wire occludes the catheter tip and is effective in reducing the reflex of injected contrast material above the level of the catheter. Experimental and clinical trials have shown significant reduction in opacification of overlying superior mesenteric and celiac vessels during retrograde aortography for evaluation of the renal arteries. Additional applications are discussed.

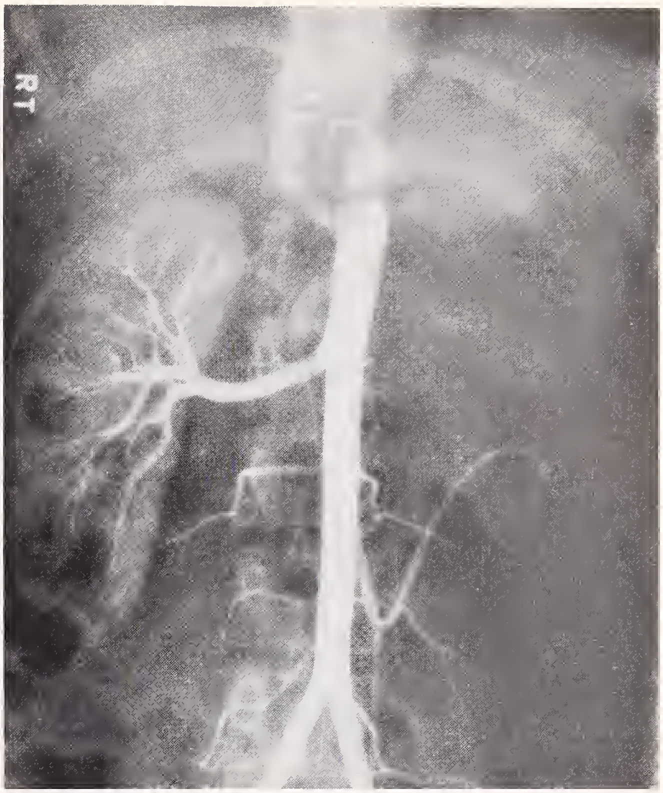


FIGURE IV

Percutaneous retrograde aortogram in 23 year old patient with congenital absence of the left kidney. The metallic plug is just below the right renal artery. Forty cc. Renovist were injected at 150 p.s.i. There is dense opacification of the peripheral renal arteries and only faint visualization of the proximal superior mesenteric and celiac vessels. The inferior mesenteric artery is densely opacified.

Addendum

During the writing of this paper the author learned of a similar modification of the percutaneous technique reported by Thornvall.[2] Although the principle is the same, there are considerable differences in the purpose and details of the system reported here, and it is felt that the advantages of this modification merit re-emphasis.

Presented in part before the New England Roentgen Ray Society; April 12, 1963, Boston Massachusetts.

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1. Seldinger, S. I.: Catheter Replacement of the Needle in Percutaneous Arteriography. Acta Radiol. 39: 368-376, May 1953.
2. Tornvall, G.: Modified Catheter for Percutaneous Angiography. Acta Radiol. 47: 470-471, June 1957.
3. Voudoukis, I. J., and Boucek, R. J.: Intercalative Renal Arteriography. Radiology 79: 82-87, July 1962.

RALPH LAWRENCE GILMAN, M.D.

Born: Boston, Massachusetts, January 16, 1902

B.A., Harvard College, 1925

M.D., Harvard Medical School, 1929

Internship: Hartford Hospital, 1929 and 1930

Staff Appointments: President of Medical Staff—Windham
Community Memorial Hospital, 1959-1960,
Willimantic, Connecticut

Fellow of the American College of Physicians

Associate member, Hartford Medical Society

Clerk — Windham County Medical Association, 1938-44
1951-52

Connecticut State Medical Society
  First Vice President
  House of Delegates, 1938-44, 1951-52
  Alternate Councilor, 1953-59
  Councilor, 1959-61
  Chairman of the Council, 1960-63
  Vice President, 1962-63

Director of Health, Mansfield, Connecticut

Medical Examiner, Mansfield, Connecticut

Medical Advisory Committee of Mansfield, Public Health Nursing Association, Mansfield, Connecticut

Member: American Medical Association
  Connecticut State Medical Society
  Windham County Medical Association

Ralph Lawrence Gilman, m.d.
President

THE PRESIDENT'S PAGE

The honor of being President of the Connecticut State Medical Society comes to relatively few and it is even less common for it to be conferred on a rural practitioner in the northeast area of the state. Hence I am doubly appreciative of this honor, and I shall try to discharge the duties and responsibilities of the office in keeping with the example and tradition of the long line of my illustrious predecessors.

I have served on the Council for some eleven years and have observed and participated in, to some extent, many activities of the Society. During this time we have had numerous serious problems with which to cope, both within our own family and also in our relationship to other organizations. We have seen many changes, even in this short space of time, in the practice of medicine and in the methods of financing medical care. I see no cessation of these problems in the forseeable future.

There is the problem of increasing specialization and the decreasing number of recent graduates who elect to go into what, for want of a better term, is labeled general practice. There are even the changing concepts of what constitutes general practice. There is very much to the fore the question of house staff for the community hospitals and the seeming monopoly of the available candidates by university connected hospitals. Add to these the increasing centralization of medical care in hospitals and what, to many, seems to be the increasing intrusion of the hospital itself into the actual practice of medicine, and we have quite a list of serious problems requiring sound reasoning and statesman-like consideration for their solution.

Then there are all the problems of third party payments for medical care—be they government, insurance companies, or Blue Shield plans. Labor and management are increasingly pushing for full coverage of all, or nearly all, medical services. The general public has become much more sophisticated insurance-wise and more and more it wants its medical care insurance to pay the whole bill. All of these socio-economic forces, to say nothing of all the political pushing and pulling that has become inextricably involved in these questions, will require many hours of study and discussion on our part. We cannot afford to let them be resolved without our active participation. Neither can we afford just to oppose changes because they are not exactly what we have been accustomed to doing.

Your officers and councilors assume a very heavy burden in conducting the affairs of your Society. They devote many, many hours and travel many miles in discharging their duties—all of which means a not inconsiderable financial sacrifice on their part. Many times we have been criticized for the decisions we have made or the policies we have adopted. Occasionally we are given a pat on the back. However, as we have gone around the state and attended the county meetings, or have conversed with colleagues at staff meetings or in the coat rooms, we have been impressed, at times even disheartened, by the widespread lack of knowledge on all these problems. Even more discouraging is the seeming apathy of large numbers towards them; the feeling that the government is inevitably going to take over so why bother to fight it; the strange belief that we shall be free to practice just as we always have when this occurs, and many similar ideas. As your President I say to you: shake off this apathy—become informed—discuss these questions with your colleagues—attend your county meetings and participate in the discussions—do not be influenced only by the few who may be most vocal in these matters—let your councilors and delegates know how you feel and what you think they should do. Only in this way can your officers and the Council truly represent the majority opinions of a strong, united profession—and a strong united profession is sorely needed in these times.

Ralph L. Gilman, M.D.

FROM THE GENERAL MANAGER'S OFFICE

William R. Richards, m.d., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS
COUNCIL MINUTES
Wednesday, March 25, 1964

I. Attendance

Present in addition to the Chairman, Dr. Martin, were: Drs. Gilman, Cullen, Goldberg, Hess, Weise, Sr., Gardner, Wilson, O'Connor, Bradley, Grendon, Grant, Davis, Phillips, Shepard, Weber, Jr., Ciccarelli, Gevalt, Egan, Abbot, Caplan, Spitz, Hastings. Also present were: Mrs. Lindquist, Mr. Burch, Mr. Nickerson and Dr. Richards. Absent were: Drs. Pitock, Scully, Hughes, Dean, Seigle, Major.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of February 20, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Stuart H. Bowman, Stamford (FCMA)
Theodore S. Evans, New Haven (NHCMA)
Charles W. O'Neill, Hartford (HCMA) beginning in 1965
Marvin E. Pearce, Texas (FCMA)
David Sussler, Norwich (NLCMA)
William R. Wilson, New Haven (NHCMA)

Resignation—Committee On Medical Care Of Veterans

It was VOTED to accept the resignation of Donn C. Barton, Portland, from membership on this Committee.

Resignation—Committee On Rehabilitation

It was VOTED to accept the resignation of Everitt P. Dolan, Bridgeport, from membership on this Committee.

Report—National Conference On Physicians And Schools

It was VOTED to approve the report filed by Joseph J. Bellizzi, Hartford, on his attendance at this Conference, October 10-12, 1963.

Request—State Commissioner Of Health

It was VOTED to empower the Chairman to appoint an Advisory Committee to the State Department of Health concerning regulations applicable to diagnostic and therapeutic X-ray equipment, in conformance with the request filed by Dr. Foote. The Chairman asked for and received several suggested names of members for appointment. The Chairman appointed: Ellwood C. Weise, Jr., Bridgeport; George P. Perakos, New Britain; John H. Woodruff, Hartford; and Alphonso DellaPietra, Middlebury.

CSMS Representative To AMA Voluntary Health Conference

It was VOTED to appoint Henry Caplan, Meriden, as the CSMS representative to attend the AMA's National Voluntary Health Conference, Chicago, September 17-18, 1964, and to authorize reimbursement to Dr. Caplan of usual expenses associated with his attendance.

III. Old, New And Special Business

Report—Committee On Hospitals

It was VOTED to refer this report on areawide hospital planning and related matters back to the Committee for further study, noting an error in Paragraph 2 (the word should be "Hospital" rather than "Medical") and to request the Committee to furnish the Council with the identity and names of the officials of the "regional hospital councils" referred to in the report. The General Manager was directed to convey to the Chairman of the Committee on Hospitals the sense of the Council's discussion of the report submitted.

It was further VOTED to have the Council undertake a study of the activities of the New Haven County Hospital Association to determine if that agency is acting in the public interest with a view toward endorsing the activities of the NHCHA if it is found to be so acting.

It was further VOTED to request the Committee on Hospitals to implement the study described in the previous action, and to make a report to the Council on its finding.

Progress Report—The Relative Value Study

Benjamin D. Thaw, Chairman of the RVS Committee, was unable to join the Council at this meeting to present his proposals for completing the Study. Dr. Thaw suggests (by letter) that the Council direct the Committee as to "steps (it) wishes it to take further." He believes that a full-time statistician should be engaged "to put together the work which has been accomplished to date and organize completion . . . of the entire remaining project (with) a physician who has the interest and full-time availability to devote to the completion of this task." It was VOTED to accept this report, with thanks. It was further VOTED to direct the Chairman of the Council to discuss these matters informally with Dr. Thaw with a view to possibly reorganizing the Relative Value Study Committee in a manner designed to expedite the completion of this project.

Report—Committee On Loan Fund

It was VOTED to accept the report of the Committee on Loan Fund concerning an application for a loan of $500.00, filed by a resident at the Grace-New Haven Community Hospital. Upon receipt of all required documents from the applicant, the General Manager's office is authorized to complete transaction of a loan in the amount stated.

Report On Joint Obs-Gyn Housing Facilities

As prepared by an Ad Hoc Committee (made up of representatives of the Society, the Connecticut Hospital Association, the State Department of Health, the Connecticut League for Nursing, and others) a report was submitted to the Council for approval. It is recommended that one or more "pilot programs" of housing clean gynecological cases on the premises of hospital obstetrical departments be implemented in accordance with certain definite rules and regulations which will be under the jurisdiction of the State Health Department.

It was VOTED to approve the report, as submitted, provided the Ad Hoc Committee is willing to delete one sentence which reads: "Only physicians who have their American Board of Obstetrics any Gynecology (certificates) or are members of the American College of Obstetricians and Gynecologists, or their equivalent, should be given this privilege." It was the opinion of the Council that local hospital staffs should determine accreditation of staff members for privileges under such programs.

Connecticut Medical Service, Inc.

The CSMS Liaison Committee with CMS filed a report on its participation in a joint meeting of the CMS and CSMS Liaison Committees held on March 23, 1964. The product of the joint meeting was contained in a series of three printed documents titled:

1. Proposed "(CMS) Bylaw Changes—Article I"
2. Proposed "Statement of Joint Understanding—1964, CMS-CSMS"
3. Proposed "Letter of Intent," describing sponsorship of CMS by the Society

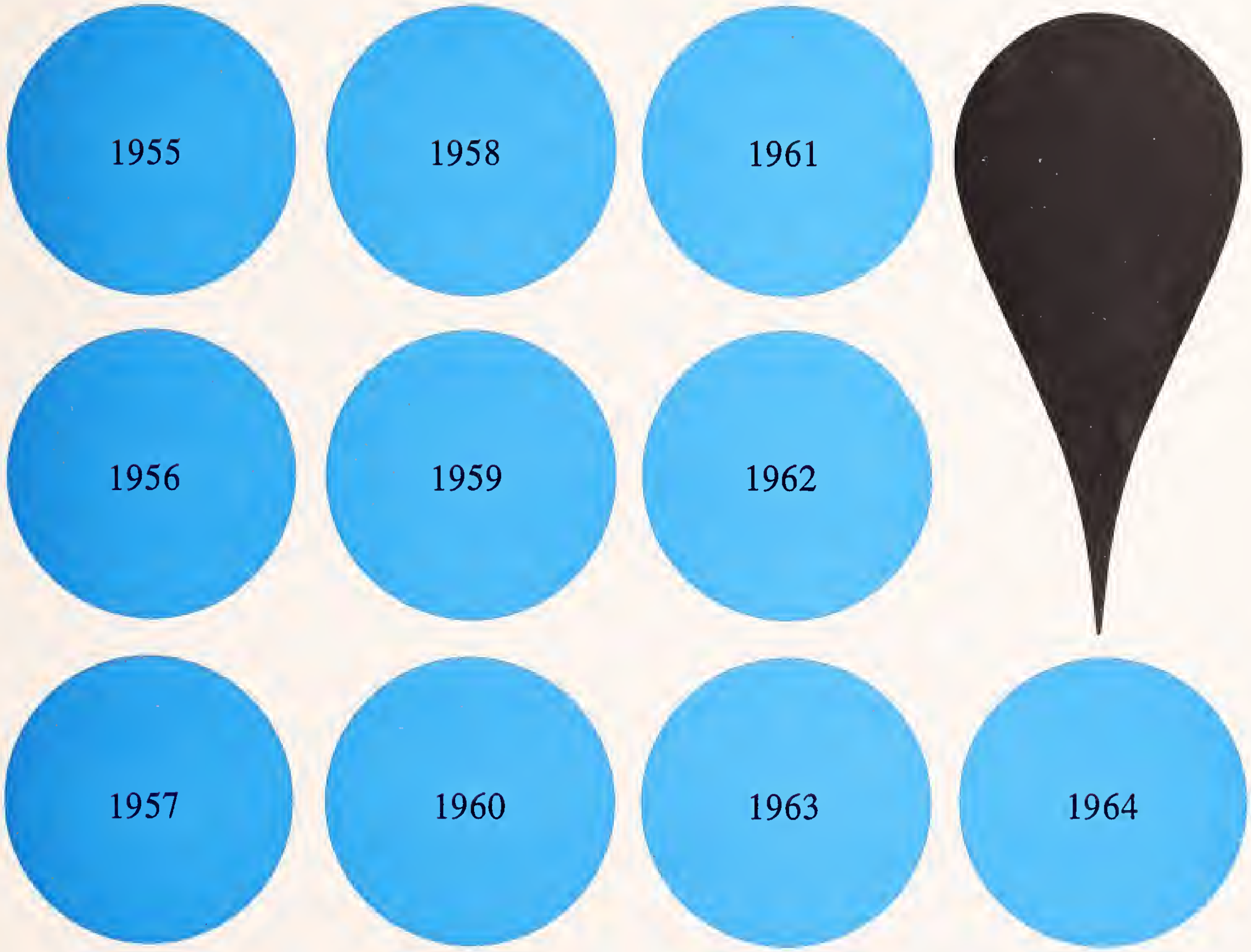
The first proposal to which the Council directed its attention was that which concerned the selection (nomination) of physician Members and Directors of CMS by the Council. A proposed amendment to Section 3 of Article I of the CMS Bylaws read as follows:

Section 3. Nominations. The President shall appoint a Nominating Committee composed of two physician Members and two lay Members who shall make all nominations for membership in the Corporation. (ADD) At least three months prior to the Annual Meeting of the Corporation, the Nominating Committee shall solicit proposals for physician-Members from the Council of the Connecticut State Medical Society. If any physician is proposed for nomination by the Nominating Committee other than those proposed initially by the Council, his name shall first be submitted to the Council, and if within thirty days thereafter the Council notifies the Committee in writing that such proposed nominee is not acceptable to it, that person shall not be nominated.

After prolonged discussion, a motion to accept this proposed amendment to Section 3, Article I, of the CMS Bylaws was lost by 8-15. A roll-call vote on the question was recorded as follows: *Yea*: Gilman, Gardner, Wilson, O'Connor, Grant, Phillips, Shepard, and Spitz. *Nay*: Cullen, Goldberg, Hess, Weise, Sr., Bradley, Martin, Grendon, Davis, Weber, Ciccarrelli, Gevalt, Egan. Abbot, Caplan and Hastings.

After additional prolonged discussion, it was VOTED to table further consideration of the report filed by the Council's component of the joint meeting of the CMS and CSMS Liaison Committees of March 23, 1964, pending further action by CMS on the position of Council stated as follows: That the Council is unwilling to consider any restoration or continuation of sponsorship of CMS by the Society which does not provide for amendment to the CMS Bylaws to restore the complete freedom of the Council to select and recall physician Members of CMS, as that privilege existed prior to June 6, 1963; that if agreement on this point is to be reached with CMS, it must be accomplished by April 8, 1964; and that, if no such agreement is

The
clear
conclusion
from
10 years'
experience...



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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

reached by that date, the Council re-affirms its intention (February 15, 1964) to recommend to the CSMS House of Delegates (on April 28, 1964) confirmation of the fact that sponsorship of CMS by the Connecticut State Medical Society no longer exists.

On this question, the vote was 20-2 in favor, with the roll-call recording the following: *Yea*: Gilman, Cullen, Goldberg, Hess, Gardner, Weise, Sr., Bradley, Martin, Grendon, Grant, Davis, Phillips, Weber, Ciccarelli, Gevalt, Egan, Abbot, Caplan, Spitz and Hastings. *Nay*: Wilson and Shepard.

Finally, it was VOTED to authorize Mr. Nickerson to informally notify Mr. Keefe of these actions of the Council and convey to Mr. Keefe the sense of the Council's discussions leading to them, and to direct the General Manager to formally notify Mr. Coolidge in writing of these same actions.

Report—Committee On Preliminary Study Of Nominations

The report of the Committee on the nominations for committees and related appointments was accepted with a few minor amendments, and it was then VOTED to approve the slate for these appointments, as amended, and to present it to the House of Delegates on April 28, 1964.

Concerning the slate of nominees for CSMS officers submitted by the Committee, the Council determined to nominate the candidates for AMA Delegate and Alternate AMA Delegate by direct vote of the Council. Accordingly, and by popular vote, nominations for these posts will be made to the House of Delegates as follows:

For terms January 1, 1965—December 31, 1966:
AMA Delegate—Stewart P. Seigle, Hartford.
Alt. AMA Delegate—Max Caplan, Meriden.
AMA Delegate—Ellwood C. Weise, Sr., Bridgeport.
Alt. AMA Delegate—Francis J. Kalaman, Norwalk.

It was VOTED to approve the balance of the slate of officers as submitted by the Committee.

It was further VOTED to refer certain matters introduced by the Committee as follows:

To the Committee to Study and Revise the By-laws:

1. Alternate AMA Delegates—the question of seating Alternate AMA Delegates as members of the Council, with full voting privilege.
2. Delegates to State and Special Medical Societies—the question of establishing criteria on which to base the selection of such delegates, and of defining the duties and responsibilities of such delegates (filing reports, etc.)

Appointment—Advisory Committee To Connecticut 65 Plan

At the request of Mr. William N. Seery, Chairman of the Executive Committee of Connecticut 65, it was VOTED to direct the Chairman of the Council to appoint an Advisory Committee to the Connecticut 65 Plan. The purpose of the Committee will be "to meet with (Conn. 65) representatives, from time to time, to consider matters of mutual interest relating to claims problems that have developed." The Chairman appointed: Ellwood C. Weise, Sr., Bridgeport; Stevens J. Martin, Hartford; and William R. Richards, New Haven.

Welfare Department Policies And Payments—CCAAGP

Fifteen members of the Connecticut Chapter of the American Academy of General Practice filed a document with the Council which outlined certain changes in Welfare Department medical policies and payments for physicians' services under Old Age Assistance and Medical Assistance for the Aged (Kerr-Mills) medical care programs which are believed to be desirable by the undersigners of the document. It was VOTED to refer the document to the Committee on Third Party Payments for study and report.

Appointment—Representative To State Narcotics Council

At the request of the Commissioner of Health, it was VOTED to direct the Chairman to appoint three members of the Society to serve as representatives to the State Narcotics Council "to consider more thoroughly medical aspects particularly related to any programs that should be undertaken for the rehabilitation of addicts." The Chairman appointed: Norman D. Gross, Hartford; Pasquale J. Costa, Jewett City; and Angelo Mastrangelo, Jr., Stamford.

Report—Public Relations Director

It was VOTED to accept as information a report filed by the PR Director on activities of his department undertaken since the last meeting of the Council. It was further VOTED to approve the recommendations of the Public Relations Division to renew the "Doctor's House Call" radio series on WBMI—FM, Meriden, for an additional twelve months' contract, at a cost of $2,344.00

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on March 25, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

Turhan Uysal, Age 33—M.D. Ankara University, Ankara, Turkey 1954. Specialty surgery.

Eli M. Isaacs, Age 31—M.D. The University of Buffalo School of Medicine. Specialty Obs-Gyn.

James E. McGrath, M.D. Jefferson Medical College 1958. Specialty Radiology.

General Surgeon, university trained board qualified, Age 33. Available July 1964.

Obs-Gyn. reaident, Age 31 – M.D. Jefferson Medical School 1959. Internship Hartford Hospital 1959-1960. Available July 1965. Interested in partnership or small single group.

PLACEMENT OPPORTUNITIES

WANTED. Pediatrician in New Haven County to take over long established practice.

FOR SALE. Pediatric practice in New Haven County.

FOR SALE. Fully equipped office with house attached, centrally located, suburb of Bridgeport.

WANTED PHYSICIANS. Hartford, Middlesex, New London and Windham Counties.

FAIRFIELD COUNTY. Physician would like to share his office with General Practitioner or Internist.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN ST., NEW HAVEN.

NEW MEMBERS

New Haven County

James A. Albright, New Haven.
Arnold J. Benton, New Haven.
Michael B. Buckley, Waterbury.
Mehdi S. Eslami, Waterbury.
Margaret L. Garrett, New Haven.
Alan H. Goodman, New Haven.
Alan R. Gurwitt, New Haven.
Gilbert F. Hogan, New Haven.
Leonard S. Krassner, New Haven.
Donald A. Nagel, New Haven.
Nicholas M. Passarelli, New Haven.
Stanley Roth, New Haven.
Edward M. Segall, Waterbury.
William M. Soybel, Hamden.
Walter R. Thayer, New Haven.
Clement J. Philbrick, Jr., Milford.
Raphael J. Torontow, Derby.
Carl F. vonEssen, New Haven.

New London County

Joseph A. Ceha, Norwich.
Peter M. Molloy, New London.
Luigi Saracino, Norwich.

Around The State

New Haven County

The 180th Annual Meeting of the New Haven County Medical Association was held at the Waverly Inn, Cheshire, Connecticut on March 19, 1964. This was preceded by a meeting of the New Haven County Hospital Association. It was announced at this meeting that 335 county physicians have registered as members to date.

With Dr. Louis C. Backhus of Waterbury presiding, the usual full program, characterizing these meetings, moved along to hold the interest of the very large audience. Honored guests introduced, committee reports, election of officers, resolutions, particularly one supporting the Council on the C.M.S. controversy, were among the highlights.

The officers elected for 1964-1965 were:

Jack Galen, Derby, President.
Luca E. H. Celentano, New Haven, Vice-President.
Hyman A. Levin, New Haven, Clerk.
Henry Caplan, Meriden, Councilor.
Frank K. Abbot, Waterbury, Senior Associate Councilor.
Waldo E. Martin, Milford, Junior Associate Councilor.
Louis C. Backhus, Waterbury, Executive Committee Member.

The meeting took note of the illness and absence of Dr. Morris H. Pitock, President of the Connecticut State Medical Society with a letter urging speedy recovery, accompanied by an appropriate token of friendship.

At dinner, following the social hour, Mrs. John J. Mendillo, Vice-President of the Woman's Auxiliary, addressed the members and their wives. Dr. Louis C. Backhus, retiring President, spoke briefly, and Certificates of Membership were then presented to recently elected members by the in-coming President, Dr. Jack Galen.

The evening closed with an illustrated lecture by Dr. Alan Dana, U.S. Public Health Service, Communicable Disease Center, Atlanta, Georgia. Dr. Dana showed slides of a recent visit to Nome, Alaska. His narration was entitled "Dog Sled Epidemiology" and was thoroughly enjoyed by everyone present.

The Problem Of Accidental Poisoning

As a step to reduce an appreciable source of preventable sickness and death, President Johnson proclaimed March 15-21 as National Poison Prevention Week. Data from the National Health Survey indicate that not far from a million people annually in the United States suffer at least one day of restricted activity or receive medical attention as a result of accidental poisoning by solids and liquids.

Fortunately, only a small proportion of these poisonings prove fatal. Nevertheless, they took 1,800 lives in 1961, the latest year for which data are available. Moreover, the death rate from this cause has increased in recent years—from 8.2 per million in 1958 to 9.9 in 1961.

The mortality from accidental poisoning among males is more than one and a half times that among females at all ages combined, the death rates being 11.6 and 7.2 per million, respectively, in 1959-60. In each sex, the danger of poisoning by solids and liquids is greatest among very young children. Among males, for example, the death rate from this cause in 1959-60 rose sharply from 14.7 per million in infancy to a peak of 57.7 at age 1; it then decreased rapidly with age to a minimum at 5-14 years. From this point the rate rose to a secondary peak at ages 45-64.

The ingestion of wood, denatured, and other alcohols is the major type of fatal accidental poisoning among males, accounting for more than a fourth of the total among them. At the same time, such lethal spirits are responsible for about one eighth of the fatal poisonings among women. Nine tenths of all the fatalities from alcohol occur in the age range 25-64 years.

Barbituric acid and its derivatives are the leading type of accidental poisoning among females, comprising one fourth of the total deaths, or twice the proportion among males. This is almost an exact reversal of the ratios for lethal alcohol. It should be noted that several times as many deaths from the barbiturates occur in California as in any other State. About one third of the fatal poisonings in each sex is caused by the ingestion of drugs and medicines other than barbiturates. Most of these deaths are caused by overdoses of aspirin and of various other analgesic and soporific drugs. Nearly 3 out of every 4 fatalities from aspirin and other salicylates occur among children under 5 years of age, while deaths from the other drugs are largely concentrated in the age range 25-64.

Children at the preschool ages account for about 90 per cent of the approximately 135 deaths caused annually in the United States by the ingestion of lead and its compounds and of kerosene and other petroleum products. Pesticides containing arsenic compounds or other lethal ingredients are also responsible for part of the death toll from poisoning among children. Caustic alkalies and acids—largely cleaning, sanitizing, and polishing products—add somewhat to the number of fatalities at the preschool ages, but deaths from these poisons occur at every period of life.

There is little doubt that the loss of life from accidental poisoning by solids and liquids can be reduced appreciably, despite a marked increase in the number of household and drug products. Most of these products are safe when used as directed, and when adequate precautions are taken to keep them out of the reach of young children. When poisonings do occur, information on the toxic ingredients of substances ingested and antidotes for them can be obtained immediately from Poison Control Centers, located in major cities throughout the United States.

Antibiotic During Pregnancy Affects Teeth Of Offspring

Antibiotics taken during pregnancy today were reported to have caused tooth discoloration and defects in several children.

Abnormal teeth were found in seven children whose mothers had taken a tetracyline (oxytetracycline, demethylchlortetracycline or tetracycline) after the fourth month of pregnancy, Allen H. Kline, M.D., Russell J. Blattner, M.D., and Martin Lunin, D.D.S., Houston, wrote in the current *Journal of the American Medical Association.*

The affected teeth showed yellow fluorescence indicating tetracycline deposits in calcifying tissues, according to the report. Six of the seven children, aged two to five, had teeth showing varying degrees of decay and incomplete enamel development.

A total of 13 children were studied, 9 from the Venereal Disease Clinic of Jefferson Davis Hospital in Houston and 4 from private practice. None had received a tetracycline since birth.

Nine of the children were born to mothers given a tetracycline or erythromycin, another antibiotic, for syphilis during pregnancy because of penicillin allergy. The private patients all received a tetracycline. All drugs were taken by mouth.

None of the four children of mothers given erythromycin in the sixth, seventh and eighth

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months of pregnancy had abnormal teeth. The other two children who had no tooth abnormalities were born to mothers given a tetracycline in the third month of pregnancy.

The pregnancy records of the four private patients were reviewed after tooth abnormalities were observed in the children, the report pointed out. The nine children of clinic cases were called in for examination because of the administration of the drugs to their mothers during pregnancy.

The dosage and duration of medication required to damage the teeth are being studied by the authors.

Of special interest was the drug history of the mother of three children included in the study, the authors said. She was given erythromycin when six months pregnant with her first child, who has normal teeth. She was given oxytetracycline when six months pregnant with her second child, who has yellow fluorescent teeth. She was given oxytetracycline when three months pregnant with the third child, who has normal teeth.

Calcification of teeth begins during the middle of the fourth month of pregnancy, the report pointed out.

"It would seem reasonable, therefore, that in this instance the tetracycline received at three months' gestation did not affect the teeth adversely because the mother received the drug before the teeth were being calcified," the authors commented.

Goiter

Goiter is an enlargement of the thyroid gland in the neck. It is usually caused by lack of iodine in the diet.

In the United States in recent years goiter has been greatly reduced by the simple expedient of adding a small amount of iodine to common table salt. In some areas of the country, such as the Great Lakes region, there is very little natural iodine in plants and water. In these areas people are likely to develop goiter unless they add iodine to the diet. The body needs very little iodine, but without a sufficient amount, the thyroid gland cannot produce a necessary substance called thyroxin. The gland thus enlarges in an effort to make up the deficit. As the enlargement continues the neck increases in size, and sometimes becomes quite large and disfiguring, as well as sometimes causing protruding eyes, increased sweating or nervousness.

Although lack of iodine is the cause of simple goiter, there are other things that can cause goiter growth, such as improper functioning of the thyroid gland or inflammation. Also, there's always the chance that the enlargement signals cancer of the thyroid.

Because of the possibility that something other than iodine deficiency is at fault, self-diagnosis and treatment of goiter can be dangerous. Your doctor will find out the true cause and will carry out the proper treatment.

If goiter is treated early, it will sometimes shrink or disappear, through proper medications. In some cases, surgical removal may be recommended, or some form of radiation may be used.

Despite iodine's importance as a preventive, it usually won't make a goiter go away once it has started.

Any swelling in the neck that might be goiter should have prompt medical attention.

Heart-Lung Machine

A heart-lung machine that runs on oxygen and is so compact that it can be carried in a car trunk has been designed and built for $1,500 by a Boston, Mass., Veterans Administration surgeon and a Massachusetts Institute of Technology engineer.

Dr. Ernest M. Barsamian, chief of thoracic surgery at the West Roxbury, Mass., VA hospital and Prof. Samuel C. Collins of M.I.T spent seven years perfecting this unit

It can be sterilized in one quick operation and primed with one quart of blood. Present, more cumbersome, machines take several hours to assemble and require three to four quarts of blood to get them going.

Heart-lung machines actually pinch-hit for those parts of the body that pump and oxygenate the blood, thus giving the surgeon time to make repairs to a damaged heart after it has been detached from the body's circulation.

Since the Barsamian-Collins machine operates on oxygen, it can be used within moving ambulances, at accident scenes, during military actions, or almost anywhere a tank of oxygen can be transported. One standard tank of oxygen will run the machine for two operations.

The machine's inventors have been putting their product through some severe tests for the past seven years at the Harvard Surgical Research Laboratory, Boston City Hospital, and West Roxbury VA hospital.

The machine has run non-stop for a whole month in an endurance try-out. It turned in an admirable performance when used on dogs, especially notable since canine blood is more fragile than human blood. Tests show further that the machine's gentle pumping action has reduced substantially the damage to red cells experienced in other machines. It is equipped also with a unique float safety device to prevent air being pumped into the blood stream.

OBITUARIES

James F. Cobey, M.D.
1892-1964

Dr. James F. Cobey, an eye, ear, nose and throat specialist for more than 40 years, died February 23, 1964 in Grace-New Haven Community Hospital after he was stricken with a heart attack at his home in Pine Orchard, Branford.

Born in New Haven, October 16, 1892, the son of John and Mary Gearns Cobey, he had practiced in New Haven since 1922, maintaining his office at 1210 Chapel Street.

He was graduated from Yale College in 1912 and Yale Medical School in 1916. From 1916 to 1917 he interned at Hartford Hospital, after which he served a year as Captain in the Army Medical Corps. Upon his discharge from the Army he served his residency at New York Graduate Hospital from 1920 to 1922.

Since 1933 he had been a member of the staff of the Yale University Department of Health. From 1953 to 1954 he was chairman of the Eye, Ear, Nose and Throat Section, Connecticut State Medical Society.

He was a member of the American Medical Association, the Connecticut State Medical Society and the New Haven County Medical Association. He was a Fellow of the American Academy of Ophthalmology and Otolaryngology and a diplomate of the American Board of Ophthalmology and Otolaryngology.

He leaves his wife, Mrs. Marie Coffey Cobey; a daughter, Mrs. Anne Cobey Spencer of Sausalito, California; a son, James F. Cobey, Jr., of Northport, N. Y.; two sisters, Miss Marie Cobey and Miss Gertrude Cobey, both of New Haven and three grandchildren.

"Jim" was loved by patients and colleagues alike, although quiet and reserved, he always had a ready smile and was truly a gentleman of the old school who will be missed by all.

R. M. Fasanella, M.D.

Augustus R. Felty, M.D.
1895 - 1964

Dr. Augustus Roi Felty was born in 1895, and died in 1964. After graduating from Yale University in 1916, he qualified for his medical degree at the Johns Hopkins University School of Medicine in 1920. He continued his post-doctoral medical training in internal medicine at the Johns Hopkins and the Presbyterian Hospitals in New York, and entered the practice of medicine in Hartford in 1924. He remained active until his retirement to Old Saybrook, Connecticut, in 1959.

Dr. Felty entered the practice of medicine at a period in American medicine when it was the exception rather than the rule for a young physician to spend four years after receiving the M.D. degree, making clinical investigations and studying patients intensively in a University Hospital environment before starting his career as an independent physician and practitioner of medicine.

During his training period he made excellent contributions to clinical medicine. His studies in acute hemolytic streptococcic infections of the throat led to a better understanding of this disease, including its mode of spread, its clinical features and its course. He attracted attention to a form of arthritis in adults which was characterized by an associated splenomegaly and leucopenia which is now known widely in the literature under the eponym of "Felty's Syndrome."

Once he entered the private practice of medicine his life was devoted to his family, his patients, and his profession. This was his full-time and life work.

He attained the high regard of his patients and of his associates through sheer strength of character and ability, through soundness of judgment, and through an innate gentleness and pervasive feeling for his fellow man. He had an unfaltering sense of responsibility which conveyed itself to his patients and his associates with vigor, but without a trace of ostentation. He practiced great medicine for the benefit of his patients. Dr. Felty embodied the highest principles of his profession; and time and again he proved his readiness to carry out those principles no matter what the cost.

All of Dr. Felty's colleagues, friends, and former patients shall miss him personally; they shall miss him professionally. To his family, all of his colleagues and associates can only say that he was one of us. We admired him, we respected him and we will treasure his memory.

Dr. Felty was a member of the Connecticut State Medical Society, the American Medical Association, a fellow of the American College of Physicians, and a Diplomate of the American Board of Internal Medicine.

He served as a Consultant in Medicine in Hartford, Middlesex (Middletown), Veterans Administration (Rocky Hill), Manchester Memorial and New Britain General Hospitals, and Cedar Crest Sanitarium (Newington).

He is survived by his widow Alice Bryce Felty, three daughters, and two grandchildren. Mrs. Jean Felty Keeney of Pittsburgh, Mrs. Sandra Felty Hansen of Houston, Texas, and Miss Kerswell Felty of Chapel Hill, North Carolina.

CHESTER S. KEEFER, M.D.

1964 MEETINGS

May 13—American Academy of Pediatrics, Connecticut Chapter, to be held at Culinary Institute, 393 Prospect Street, New Haven, at 7:00 P.M. Speaker: Dr. Robert Kugel, Prof. of Medical Sciences, Brown University, Providence, R.I.

May 20—Annual Meeting Connecticut Heart Association to be held at Hillandale Country Club, Trumbull.

May 25-27—Annual Meeting American Thoracic Society Medical Section of the National Tuberculosis Association to be held in New York City.

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

In Memoriam

Buckley, Richard C.—Hartford; Yale Medical School, 1924. Dr. Buckley was chief of neurosurgery at St. Francis Hospital, Hartford. He was associated with Dr. Harvey Cushing, professor of neurosurgery at Harvard University following internship at Peter Bent Brigham Hospital. Dr. Buckley was a member of the Harvey Cushing Society, the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. He was a diplomate of the American Board of Neurosurgery and a Fellow of the American College of Surgeons. Dr. Buckley died March 18, at the age of 66.

Cohen, David J.—Meriden; Yale School of Medicine, 1932. Dr. Cohen was chief of staff and director of Medical Services at the Meriden Hospital. He was president of the Meriden Heart Association and former president of the Meriden Medical Society. Dr. Cohen was a member of the American Academy of Pediatrics, the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, and the Meriden Medical Society. He was certified by the American Board of Pediatrics. Dr. Cohen died April 1, at the age of 57.

Loffredo, Louis — Middletown; Pennsylvania University School of Medicine, 1922. Dr. Loffredo served as chief of surgery at Middlesex Memorial Hospital from 1929 to 1937, when he founded his own hospital—"Crescent Street Hospital," in Middletown. He was a member of the American Medical Association, the Connecticut State Medical Society, the Middlesex County Medical Association, the Middlesex Memorial Association, and the Bassini Surgical Society. Dr. Loffredo was a Fellow of the American College of Surgeons. He was a member of the Middletown Board of Health for more than 25 years and the Middletown Board of Education for nearly 10 years. He also served as police surgeon. Dr. Loffredo died March 25, at the age of 69.

WOMAN'S AUXILIARY

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Annual Auxiliary Meeting

The twentieth annual meeting of the Woman's Auxiliary to the Connecticut State Medical Society was held Wednesday, April 29 at the Tumblebrook Country Club in Bloomfield. A morning business session was followed by a luncheon, with William B. Walsh, M.D. president of Project HOPE as the guest speaker.

The slate of officers for 1964-65 headed by Mrs. Charles M. Krinsky of New London as president was installed at this time.

Delegates and alternates to the National Auxiliary Convention in San Francisco, June 21 to 25 were elected, as were the members of the nominating committee for the coming year. Reports of the counties and various committees of the Auxiliary were given to the members.

Notes Of Interest

The fifth meeting of the Board of the Auxiliary was held on March 16 at the Carriage Drive in Hamden with twenty Board members present. The state budget for 1964-65 was approved and recommended for adoption by the Auxiliary at the annual meeting April 29th.

Mrs. Charles M. Krinsky, president has been appointed to the Connecticut Health League as a delegate for a term of three years.

The AMA-ERF chairman, Mrs. Winfield Wight has reported that New London county has been commended by both the Eastern Regional Chairman and the National Chairman for their recent fund raising drive, the showing of the play "Rebecca," as a novel approach.

The Health Careers chairman, Mrs. Edward P. Allen has alerted the Auxiliary to watch for forthcoming news releases on this subject which have been sent to representative newspapers throughout the state. Health occupations now occupy third place in the nation's working force while a short ten years ago these occupations ranked in seventh place.

The Legislative committee urges all members to take a participating interest in elections.

The AMA-ERF Loan Guarantee Fund was voted a donation of $150 from the State Auxiliary.

FORTY-FIRST NATIONAL CONVENTION
Woman's Auxiliary to the American Medical Association
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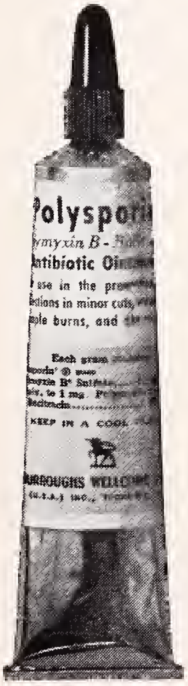

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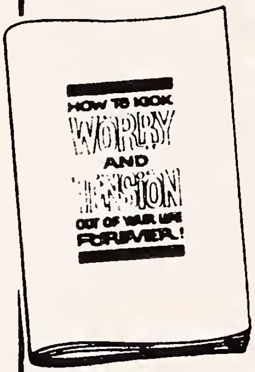

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Special Notices

POSTGRADUATE COURSE IN MEDICAL EDUCATION

New York University Medical Center

New York City, June 10-12, 1964

"3 Days of Cardiology," a postgraduate course in medical education, titled "Hemodynamic Basis for Auscultation" will be held in New York City, June 10-12, at the New York University Medical Center. Drs. J. Scott Butterworth and Edmund H. Reppert will co-direct the course.

Sponsored jointly by the Council on Clinical Cardiology, American Heart Association and New York University Medical Center, the course has been designed for Cardiologists, Internists, Pediatricians, and others interested in the advances made in the past decade in Auscultation and in a review of the physiologic basis of heart sounds and heart murmurs.

For more information, contact your local Heart Association.

COUNTY-WIDE PSYCHIATRIC MEETING AT HALL-BROOKE HOSPITAL

Thirty-two psychiatrists from Fairfield and Litchfield Counties met at Hall-Brooke Hospital in Westport on April first to organize a Chapter of the Connecticut District Branch of the American Psychiatric Association.

For many years the psychiatrists have been meeting on a state-wide basis. However, with the growth of psychiatry, and the recognition of the need for the professional person to be involved with local community problems and needs, Connecticut has been divided into three geographical areas, Hartford, New Haven-Middlesex, and Fairfield-Litchfield.

At the Hall-Brooke Hospital meeting plans for the future were discussed and the following officers elected:

President: Leo H. Berman, M.D., of Westport and Norwalk.
President-elect: Walter W. Kemp, M.D., of Stamford.
Secretary: Albert M. Moss, M.D., of Fairfield and Westport.
Treasurer: Faith N. Ogden, M.D., of New Canaan.
Councillors: William B. Rich, M.D., of Torrington.
Elwyn M. Smolen, M.D., of Bridgeport.
Paul E. Kaunitz, M.D., of Westport.

AMERICAN ASSOCIATION OF ELECTROMYOGRAPHY AND ELECTRODIAGNOSIS

August 23, 1964

The Annual Meeting of The American Association of Electromyography and Electrodiagnosis will be held on Sunday, August 23, 1964, at the Statler-Hilton Hotel, Boston, Massachusetts.

Please address all communications to: Max K. Newman, M.D., 16861 Wyoming Avenue, Detroit, Michigan 48221.

Letters To The Editor

To The Editor:

The Editorial "Salt, Genetics and Hypertension" which appeared in the February issue of CONNECTICUT MEDICINE, was most informative, scientific and with a practical application for Preventative Medicine.

Thomas Chandler Haliburton 1843 in his book "Wise Saw" is first given credit for the saying: "An ounce of prevention is worth a pound of cure." Apropos this article "Less than 3 grams of salt a day may keep hypertension away."

Prevention is one formidable pillar of strength in medicine. The physician in general and the pediatrician in particular aim for optimum growth and development by immunization against contagious and infectious disease and by proper protective diets to obviate nutritional deficiences and by accident prevention information, etc.

The allergists advise that where there is a family history of major allergy, the mother is urged to breast feed her newborn or use a milk free substitute; to avoid adding highly allergenic foods early in life, and to give careful consideration to environmental factors so that the development of allergic symptoms may either be delayed or prevented.

The author should be commended for emphasizing prevention in this and the many other areas of medicine where the hereditary factor is present.

JOSEPH WEINER, M.D.

New Haven, Conn.

To the Editor:

I am taking the liberty to attract your attention to an article of mine entitled "Fever as a Defense Against Disease" which appeared in the April issue of the *Journal of the American Geriatrics Society*.

I believe that this article would be of great interest particularly to those physicians who keep prescribing aspirin to bring fever down.

MARCEL THAU, M.D.

Hartford, Conn.

To the Editor:

I've mentioned once before to you how much I like your editorial section. These, and those by Dr. Page in *Modern Medicine*, are my favorites.

I want to tell you how much I appreciate your mention of our little symposium. I guess you've also noticed how difficult it is to get the men to write.

Your mention, plus your original letter, helps a lot.

Sincerely yours,

J. A. FABRO, M.D.

Torrington, Conn.

Symptomatic Treatment of Diarrhea

Preparations offered for the symptomatic treatment of diarrhea include such drugs as bismuth and aluminum salts, activated charcoal, kaolin, pectins, tannins, hydrophilic gels and prepared chalk. Many proprietary preparations are combinations of two or more of these agents. The antidiarrheal effects of such preparations have variously been attributed to a "demulcent" or "coating" effect, to astringent action, to inhibition of bacterial growth, and to adsorption of toxins. Whatever the mechanism, the drugs are often employed for symptomatic relief in both mild and severe diarrheas. In the absence of controlled trials, it is difficult to determine what value they have in mild diarrheas, which are usually self-limited and brief without treatment. In the severe acute diarrheas and in chronic diarrheas, as in ulcerative colitis and ileitis, they are ineffective.

KAOLIN; ATTAPULGITE — Perhaps the favorite over-the-counter and prescription remedy for symptomatic treatment of diarrhea is Kaopectate (Upjohn), a combination of kaolin and pectin. It is similar in composition to Kaolin Mixture with Pectin NF. This type of preparation was introduced several decades ago, and has the sanction of long usage if not of controlled trials. A preparation recently introduced for symptomatic treatment of diarrhea is attapulgite compound (Quintess-Lilly). Each fluid ounce contains 3.9 Gm. of attapulgite, a hydrous magnesium aluminum silicate, and 0.3 Gm. of a pectin. According to the manufacturer, *in vitro* laboratory tests have shown "activated" attapulgite to be "superior to kaolin as an adsorbent for certain alkaloids, toxins, bacteria, and strains of human enteroviruses." What relation *in vitro* adsorbent properties have to diarrhea and other symptoms is not clear. No clinical trials demonstrating superior symptomatic effects have been reported.

Quintess-N is the same drug combined with Neomycin Sulfate USP. The manufacturer recommends Quintess-N for the treatment of "acute bacterial diarrheas due to enteropathogens susceptible to neomycin sulfate, particularly Salmonella, Shigella, certain types of Esch. coli, and staphylococci." Neomycin is not the drug of first choice for Salmonella infections, Shigella or staphylococcus enterocolitis; while it is often effective against enteropathogenic E. coli (EPEC) organisms, resistant strains are frequently encountered.

OTHER COMBINATIONS—Some of the prescription drugs offered for diarrhea combine demulcents with opium derivatives. Others combine hydrophilic gels with anticholinergic agents, as in White Laboratories' Sorboquel (see The Medical Letter, 3: 66, 1961, for an evaluation of this drug). A later review of various anticholinergic agents (Medical Letter, 4: 30, 1962) said that "there is no satisfactory proof that anticholinergics are more useful than placebos" in functional gastrointestinal disorders. Although hydrophilic gels (Mucilose, etc.) are primarily prescribed for constipation, their water-binding properties suggest their possible usefulness in diarrhea; while they are reported to be effective, controlled studies are lacking.

Lomotil (Searle), an oral mixture of diphenoxylate hydrochloride (a synthetic narcotic) and atropine sulfate, was introduced in 1961 for the symptomatic treatment of acute and chronic diarrhea. Though the addiction liability of diphenoxylate is comparable to that of codeine, the *mixture* is classed as an exempt narcotic in the United States. The Medical Letter (3: 61, 1961) stated that "If the effectiveness of Lomotil in giving symptomatic relief of severe chronic diarrhea is established by carefully controlled trials, and if the addiction record continues to be favorable, Lomotil will be a useful alternative to opiates." The addiction record of the drug continues to be favorable but, unfortunately, controlled trials in chronic diarrheas have not been reported. Like opiates, Lomotil does reduce propulsive motility of the intestines. For symptomatic relief of acute diarrhea, there is no evidence that it is more effective than appropriate doses of Camphorated Opium Tincture USP or a codeine drug. There is no danger of addiction from the temporary use of an opiate for acute diarrhea; even in chronic recurring diarrhea, intermittent use of an opiate is generally safe. For persons of unstable personality, or prone to addiction, however, Lomotil is probably preferable.

RECOMMENDATIONS — Mild diarrheas of bacterial or viral origin are usually self-limited and, in most instances, require neither specific chemotherapy nor symptomatic treatment. If desired, a demulcent can be used, and the patient can refrain from eating fruits and vegetables or other foods with residue. Sweetened tea and toast are foods traditionally prescribed in acute diarrhea. For the symptomatic relief of severe, acute diarrhea, an opiate is more likely to be effective than a demulcent (in infants, these drugs are usually not needed; at most a sedative should be prescribed). In severe diarrhea due to chronic ulcerative colitis, corticosteroids not only give symptomatic relief but also result in

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general improvement in the patient's condition (Medical Letter, 4: 27, 1962).

In severe infectious diarrhea, antimicrobial therapy is often necessary, but derangements of water and electrolyte balance may be more serious hazards than the infection itself, and where the diarrhea continues for more than a few days (less in infants and elderly persons), control of water and electrolyte balance may be far more urgent than the use of antimicrobial drugs. In an infant, when severe diarrhea continues for more than a few hours, solid food should be restricted, and the infant given sugared water and an oral electrolyte mixture every hour or so, or as frequently as needed to insure adequate urine output.

A useful homemade oral fluid formula is ¼ teaspoonful (or about 1.5 Gm. each) of sodium chloride and sodium bicarbonate and 50 to 100 Gm. ordinary sugar, according to caloric requirements, per quart or liter. If there is concern about potassium loss, as in prolonged diarrheas, about 1.5 Gm. of potassium bicarbonate may be added to the formula. A proprietary preparation—Lytren powder (Mead Johnson)—furnishes approximately the same amounts of sugar and electrolytes, including both sodium and potassium, as the homemade formula; for use, 80 Gm. is dissolved in a liter of water. "The usual precaution of withholding potassium until the patient has voided seems advisable" (C. E. Brooke and C. S. Anast, J.A.M.A., 179: 792, 1962). If oral feedings are not feasible or the patient is very ill, parenteral fluids should be administered.

Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y., Vol. 5, No. 16, August 12, 1963.

Study Suggests Link Between Body Build And Ulcer

A study of Yale University men suggests that there may be a link between body build and susceptibility to ulcer.

The study was reported by Drs. James C. Niederman, Howard M. Spiro and William H. Sheldon, Yale University School of Medicine, New Haven, in the current *Archives of Environmental Health*, published by the American Medical Association.

The slender, linear physique, or ectomorphy, was found to be associated with a higher blood level of pepsin, an enzyme contained in the gastric juice, considered an indicator of ulcer-proneness.

An ulcer was recognized in 14 of 931 Yale freshmen, aged 16 to 21, during the four-year study.

The levels of blood pepsin in those who developed ulcer disease were "significantly higher" than in those without the disease although the actual number of cases was small, the physicians said.

Eleven of the 14 patients had either high or high normal blood pepsin values. The other three cases had low normal values, but in no case did a person with a low blood pepsin develop ulcer disease, according to the report.

This finding supports earlier investigations that blood pepsin measurements may be useful as a marker of susceptibility to ulcer disease, the authors said.

A gradual increase in the mean level of blood pepsin was found to be associated with increasing degrees of ectomorphy, according to the report.

On the other hand, increasing degrees of endomorphy, roundness and softness of build, tended to be associated with decreasing pepsin levels. No definite association was apparent with mesomorphy, a muscular and bony physique.

The association of pepsin levels with ectomorphy "requires further exploration, but raises pertinent questions regarding the possible role of a body build factor in the pathogenesis of duodenal ulcer," the authors concluded.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Cancer Of The Stomach. By William H. ReMine, M.D., James T. Priestley, M.D., Joseph Berkson, M.D. and Members of the Staff of the Mayo Clinic. W. B. Saunders Company, Philadelphia and London, 1964. 255 pp. $11.50.

Case Studies In Obstetrics And Gynecology. By F. Jackson Stoddard, M.D. W. B. Saunders Company, Philadelphia and London, 1964. 312 pp. $8.50.

Gastroenterology. By Henry L. Bockus, M.D., Volume 2, W. B. Saunders Company, Philadelphia and London, 1964. 1241 pp. $28.00.

Handbook Of Legal Medicine. By Alan R. Moritz, M.D. and C. Joseph Stetler, LL.B., LL.M., Second Edition, The C. V. Mosby Co., St. Louis, 1964. 218 pp. $5.75.

Towards Earlier Diagnosis. By Keith Hodgkin, M.D. Forward by Sir Robert Platt, M.D., E. & S. Livingstone Ltd. Edinburgh & London, 1963. 447 pp. $6.50.

BOOK REVIEWS

PHYSIOLOGY OF THE CIRCULATION IN HUMAN LIMBS IN HEALTH AND DISEASE by John T. Shepard, M.D., W. B. Saunders Co., Philadelphia, Pa., 1963, 416 pp., $12.00.

Reviewed by: LOUIS H. NAHUM

This is a book by a Professor of Physiology at the Graduate School of the University of Minnesota School of Medicine and brings together all the information which has accumulated especially in the last ten years on circulation through the limbs. But it does not forget the general mechanisms of the body that control the circulation and it analyzes and correlates the available data in a field that has become increasingly complex.

There are four sections with a total of forty-one chapters. Section I deals with the nervous control of blood vessels. Section II covers the local factors that control blood vessels. In section III there is a thorough analysis of humoral control of blood vessels and in section IV the author has brought all the above basic physiology to bear upon an understanding of blood vessel activity as they are modified in various disease states all the way from Raynand's through occlusive diseases and finally deformans.

Each chapter begins with a synopsis of the points covered in the chapter and ends with a very extensive bibliography of the experimental work upon which the author has based his conclusions.

The book is a highly specialized part of physiology and should appeal to those physicians who wish to understand clinical medicine from the dynamic standpoint. This reviewer can think of graduate students whose major interest is in the cardiovascular system as beneficiaries of this excellent treatise. A young investigator who is searching for fruitful areas for study will be greatly helped and stimulated by thorough familiarity with this book. An experienced investigator and teacher in physiology will find this book an excellent source of information. Finally since the book is a basic text on the behavior of human blood vessels in health and disease, it can be an excellent stimulus to the clinician whose interest is in diseases affecting the vascular system.

HISTORY OF THE MEDICAL DEPARTMENT, UNITED STATES ARMY, Editor-in-Chief, Col. John Boyd Coates, Jr., MC, USA.

ORGANIZATION AND ADMINISTRATION, Editor, Charles M. Wiltse, Ph.D., Litt.D., Superintendent of Documents, U.S. Gov. Printing Office, Washington, D. C., 613, pp., $6.25.

PERSONNEL IN WORLD WAR II, Editor, Charles M. Wiltse, Ph.D., Litt.D., Superintendent of Documents, U.S. Gov. Printing Office, Washington, D. C., 548 pp., $6.00.

The above two volumes have been reviewed together inasmuch as they are two sides of the same coin.

Reviewed by DENIS S. O'CONNOR

ORGANIZATION

It would be impossible in the space available for this review to even comment on the detailed problems of the organization of the Medical Department of the Army in World War II.

When one realizes what it meant to build up a Medical Department for the service of a peace-time army of about 200,000 men to one to give medical service under combat conditions all over the globe to an army of 8,000,000 including recruitment, training, supplies, hospital and medical depot planning and construction and many other less obvious duties one can conclude that to have come through the war with little criticism was a notable achievement.

It would seem that basic organization of the War Department should be so thoroughly studied in peace time that in time of emergency violent changes in the organization would not complicate an otherwise stupendous undertaking. Nevertheless, that is what happened. A sweeping re-organization of the War Department early in 1942 moved the Surgeon General from Staff Headquarters to the intermediate Service of Supply. When one considers, the many activities of the Medical Department of the Army one can appreciate some of the reasons for this placement of the Surgeon General's Office but when one realizes the importance of the main function of the medical department—the provision of the highest type of medical care for the combat troops—one can realize the dismay of the Surgeon General and the officers of the department of the regular army. It is to the credit of the Surgeon General's Office and the theatre surgeons that with full loyalty to the changed position which made their work so difficult they ingeniously improvised a relationship, especially in the European Theatre that the surgeon responsible for the medical care in that important theatre was able to be in effect the surgeon on the headquarters staff.

Another difficulty which interfered with the smooth functioning of the Surgeon's office was the constant harassment by the Air Force for a separate medical department. Even with full understanding for and sympathy with the Air Force Problems, one can only feel that it was most unfair to make the Surgeon General's burden so much more difficult. The loss of control of the general hospital by the Surgeon General was still another complicating factor in his control of medical activities.

While the functioning of the Medical Department in a land area such as the European Theatre presented no unusual problems the Pacific area was another matter. Here they were dealing with numerous small land areas widely separated in a vast expanse of water. It was difficult to apply the table of organization to this area and the inflexible character of Army organization made adequate placement and use of army personnel difficult.

The disease problems, especially that of malaria which constituted a serious threat to the effectiveness of combat troops in so many scattered areas of the world required a separate organization to survey infected areas, to identify vectors, eliminate breeding grounds, protect troops and suppress symptoms.

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The recruitment of personnel for the medical department complicated by the civilian and military requirements was a constant problem for the Surgeon General. Medical and hospital supplies in hitherto unheard of amounts and distribution to needed areas all over the globe, the training of personnel, the advantageous assignment of personnel throughout the world, the meeting of official and unofficial criticism were only a few of the Surgeon General's problems. When one saw how little sometimes it took to put an enlisted man, or officer, on the psychiatric list, one wonders how the individual holding the office of Surgeon General withstood all his tribulations.

The very fact that the medical department came through so splendidly the severe test which World War II presented to it should give lasting satisfaction to those who shared the top echelon of that department.

PERSONNEL

The volume on "Personnel in World War II" views the medical department from the many problems connected with the recruiting, training and assigning of the different corps of officers and enlisted men, the problems of putting the right person in the right place; keeping everyone happy or at least trying to appease unhappiness; battling the community agencies which were unwilling to surrender necessary professional personnel to military necessity, meeting the reluctance of the individual to accept military service and assuring the political representatives of their appealing constituents that the individual was being accepted at his own evaluation and was being treated in a manner consistent with his place in civilian life.

Doctors of medicine, the group which constituted the largest corps in the medical department, constituted a constant recruitment problem throughout the war. The industrial expansion which was necessary to meet the needs not only of our own military establishment but also of our allies, not only made the civilian sector financially attractive to the doctors but also gave them the feeling of contributing to the war effort. Family and financial responsibilities, the acquisition of a position in the profession attained only after years of effort and sacrifice as well as other consideration operated to develop a reluctance on the part of some doctors to enter the military service voluntarily or to accept service when certified as available.

Specialization in medicine which had become the rule rather than the exception since World War I aggravated the above factors and a specialty itself, such as obstetrics, sometimes seemed to rule out any military usefulness. The unhappy placement and apparent lack of need reported by some who had volunteered or had been recruited only served to give those unwilling to serve an argument against accepting service.

Unquestionably, many of the duties to which doctors were assigned could have been done as well, if not better, by persons trained in business or hospital administration. But, if the table of organization called for a doctor of medicine one had to be assigned to it. It will have to be recognized that it takes six years to make a doctor and in time of war the civilian needs for doctors will be increased and those doctors who are called by the military must be placed and used to the optimum capacity. Unfortunately, a specialty in medicine by limiting the usefulness of the individual doctor will make the effectiveness of some doctors less. This is a matter to which the military must give thought.

Rank also proved to be a problem in placement as well as in morale of the corps. It was found not infrequently that a doctor with qualifications for a position did not have the military rank for the position. The dissatisfaction of doctors with their military rank was the source of much trouble. Nothing short of obliteration of military rank can solve either problem.

Dissatisfaction with placement and optimum usefulness was greater in the Pacific Area than in the European Theatre. The inflexible nature of the army organization was responsible for this and under similar circumstances a modification of the army organization will have to be worked out.

The volumes on organization and on personnel are interesting from the viewpoint of the overall problems. They could well be required reading for regular army medical personnel and could well be the textbooks for those who should be concerned with the personnel problems and organization of the medical department in a future war. Certainly, the basic organization for war time use should be spelled out well in advance of its need rather than to be imposed on its officer personnel at a time when they must give full consideration to the problems incident to mobilization.

GARROD'S INBORN ERRORS OF METABOLISM, reprinted, with a supplement by Harry Harris, M.D., Oxford University Press, London, 1963, 207 pp.

Reviewed by: HERBERT LEVINE

The vast expansion of biochemical genetics in recent years is aptly illustrated by this volume. It contains the text of Archibald E. Garrod's classic monograph, "Inborn Errors of Metabolism." first published in 1909, and a supplement by Harry Harris which succinctly summarizes the developments in the field since Garrod's time. The original text was concerned with albinism, alkaptonuria, cystinuria, and pentosuria. Garrod considered these disorders to be characterized by genetically determined deficiences of specific enzymes. Modern biochemistry has confirmed his view, and its techniques have located precisely the sites of these deficiencies in the metabolic pathways involved. Cystinuria, however, is due to a defect in amino acid transport processes rather than an enzyme deficiency. The "one gene, one enzyme" concept of recent biochemical genetic interest has its roots in Garrod's work.

Harris' essay discusses the sites of metabolic block in Garrod's original group of errors, and describes the precise biochemistry of a number of other genetically determined conditions. Sex chromosome inheritance is illustrated by glucose —6—phosphate—dehydrogenase deficiency, a sex-linked trait that results in hemolytic anemia in response to such drugs as primaquine. His discussion of this topic includes current views of dosage compensation, and the Lyon hypothesis and its implications are well described. The genetic determination of structure in proteins which are not enzymes is exemplified in a discussion of the abnormal hemoglobins.

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This volume provides an excellent introduction to biochemical genetics for the physician by combining the text of Garrod's classic work in the field with Harris' fine summary of recent developments.

MAN AND HIS FUTURE. Edited by Gordon Wolstenholme. A Cabi Foundation Volume. Little Brown & Co., Boston, Toronto, 1963, 410 pp. $6.00.

Reviewed by: LOUIS H. NAHUM

This book is charming because it contains the thoughts and speculations of twenty-seven of the outstanding scientists —several of whom are Nobel prize winners of our generation. And so we find expressing themselves: Sir Julien Huxley, J.B.S. Haldane, Carleton Coon, Gregory Pincus, Albert Szent-Ceyjorgi, Herman J. Muller, Joshua Lederberg, F.H.C. Crick, P. B. Medawar and many others.

Generally Ciba Symposiums are small international conferences concerned with highly technical, specialized and fundamental aspects of medical reseach. This book, however, is an exchange of opinions about the future of this world. The reason for this is, that our present world was unprepared socially, politically, and ethically for the advent of nuclear power and its great potential for evil. The world is also unprepared for new biological research which is creating methods of interference with natural processes which could destroy or transform nearly every aspect of human life which we value.

This has made urgently necessary for every intelligent individual and every social system to consider the present and imminent possibilities. Since it is the scientist who is transforming the world, it must be the scientist alone who can bring these matters to the attention of government and guide them towards fashioning a happier and healthier world. In short, the two independent worlds of science and of letters which C.P. Snow has so beautifully portrayed must be reconciled and unified.

It is clear to all of us that there exist a separate system of ethics for individuals from that of governments. The system of ethics for individuals we all subscribe to. Somehow we don't seem to expect our governments to subscribe to the same set of ethics. Unless governments also became civilized, the world is likely to perish. But how to make governments civilized?

All contributers agreed that we are on the threshold of a truly critical step, into the phase of self conscious evolution. They felt that we are now in a position to make a new major advance in education by educating people in the evolutionary concept and in the ecological concept. Both are turning out to be very important ways of organizing our thinking about life and its environment. Presumably, to influence governments away from their anarchical approach to life on this planet, there needs to be a new individual who can only be prepared by a radically reorganized educational system.

What the impact of such a book will have upon people and governments cannot be predicted. It is hoped however, that the people who contributed to this symposium will be able to personally influence leaders of education and leaders of government to listen to the lesson they here offer. For these contributions are by the workers who are shaping the future of science. What they think about the world of today, and what the world of tomorrow will be or can be like cannot be lightly passed aside either by individuals or by governments.

YOUR CHILD STEP BY STEP TOWARD MATURITY by Dorothy Noyes Sproul, Doubleday & Co., Inc., Garden City, New York, 1963, 274 pp. $4.50.

Reviewed by: IRA S. GOLDENBERG

What are the prerequisites for an author of a volume on child rearing? A medical degree and extensive experience as a pediatrician? Prolonged exposure to the problems of children as a social psychologist? Or a rational knowledge of one's own experiences "just" as a parent? Dorothy Noyes Sproul is neither a physician nor a sociologist, but rather a former advertising executive who brought two children through the rigors of childhood and has gained insight and wisdom which she now set down in this thoughtful and fact-filled book. Her syndicated column dealing with the health problems of youngsters has been widely circulated and the present book represents a distillation of much of the material from these columns.

Mrs. Sproul has analyzed the health problems of children and has done a remarkably able job of conveying in a straight-from-the-shoulder manner the importance of preventive medicine, including the ever present threat of accidents—childhood's greatest killer. A carefully administered initial dose of "safety vaccine" is recommended, with almost continual boosters as the child grows. The discussions related to a parent's role in developing intellectual, spiritual and emotional strength in the child are particularly valuable to all parents in this age of atomic unrest. This is a book for every parent, and is recommended unequivocally to all physicians who should, in turn, recommend it to all parents and parents-to-be.

The well established Dr. Spock has been joined by an individual who expresses herself with brevity and commonsense and recognizes above all that we should listen to children more than we usually do. Mrs. Sproul's introduction states that, "Children are our greatest asset, our greatest natural resource. Without them, no tomorrow has any significance." Her book forcefully tells how to preserve this asset for a greater tomorrow that sometimes seems impossible today.

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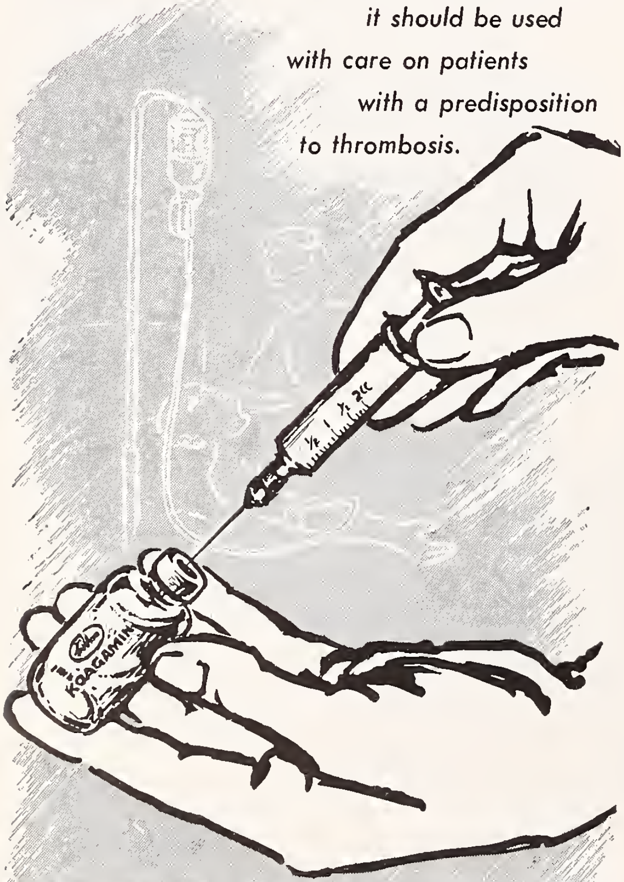

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DISEASES OF THE CHEST by H. Corwin Hinshaw, M.D., Ph.D., D.Sc., and L. Henry Garland, M.B., B. Ch., M.D., Second Edition, W. B. Saunders Company, Philadelphia, Pennsylvania, 1963, 789 pp. $20.00.

Reviewed by: LOUIS H. NAHUM

In the last six years so many changes have occurred in the treatment of tuberculosis; viral infections of the respiratory tract have become much better known; the clinical significance of the facts of pulmonary physiology have become more evident; much experience with bronchogenic cancer has accumulated, and nearly every other aspect of diseases of the chest has been modified in some manner. As a result, extensive revision of the first edition has become urgent, so also introduction of entirely new material.

The book consists of thirty-eight chapters covering diagnostic procedures including clinical history, evaluation of complaints, physical examination, bronchoscopy, biopsy laboratory studies, anatomy, and pulmonary function tests, and various diseases. Each chapter is followed by important references and at the end is a good index.

Three additional contributors appear in this edition. Clinical application of pulmonary function testing by Assistant Professor Charles T. Carman; foreign bodies in the tracheobronchial tree by Assistant Professor Walter E. Heck and coccidioidomycosis by William A. Winn, Medical Director, Tulare-King's Counties Hospital, Springville, California. As for the remainder of the work, it is a perfect example of team work between an internist of wide experience in teaching and practice, and a radiologist. This is a happy combination, especially in producing a first rate book on diseases of the chest. The text is based upon personal observations and experience of many years in clinical research.

The figures are excellently reproduced and important aspects clearly emphasized by overset drawings. The paper and printing is of very high caliber.

This book is recommended for all students, internists and thoracic surgeons as being the most authoritative in this field.

THE PLASMA MEMBRANE

Reviewed by: WILLIAM F. ECKHARDT, JR.

The Symposium on the Plasma Membrane published by the American Heart Association was first included as a November, 1962 supplement to Circulation, the journal of the American Heart Association, and is the outgrowth of a two day symposium held under the auspices of The New York Heart Association.

It was post-hoc dedicated to the memory of Dr. Homer W. Smith, a leader for years in the field of renal physiology.

For the non-basic science oriented physician, the entire 241 pages make very difficult reading. Since the concept of the cell membrane is now permeating clinical medicine, some of the papers are must reading for the clinician who strives to be knowledgeable.

I would heartily recommend that all readers who enjoy biological literature read Dr. Homer Smith's brilliant and joyfully written review, "The Plasma Membrane, with Notes on the History of Botony." There are also murky, technical reviews of cell osmometry and membrane potentials, and results of X-ray difraction and electron microscopic studies of the membrane.

Dr. Don Fawcett of Harvard Medical School Department of Anatomy has clearly reviewed the fascinating cell surface specializations of the membrane and has speculated how structure and function are related. This is the shortest and clearest reveiw of small intestinal cell, renal cell and exocrine cell functional morphology that this reviewer has read.

For most physicians, The Symposium on the Plasma Membrane may tell them more about the cell membrane than they care to know. To the cellular physiologist and the basic science worker in the clinical sciences, it is an excellent review of work in the field as of 1961. To all even vaguely interested in biology, Drs. Smith and Fawcett's papers are strongly recommended.

THE TRANSITIONS FROM ANCIENT EGYPTIAN TO GREEK MEDICINE by J. B. deC. M. Saunders, M.D., University of Kansas Press, Lawrence, Kansas, 1963, 40 pp., $2.00.

Reviewed by: HERBERT LEVINE

This thin volume of 40 pages contains the tenth series of Logan Clendening Lectures in the History and Philosophy of Medicine. This lectureship was established at the School of Medicine of the University of Kansas in 1949, and the first lecturer was John F. Fulton. In the current lecture Dr. Saunders explores the Egyptian roots of certain specific and general aspects of Greek medicine. He points out that the achievements of anicient Greece did not arise de novo, and that continuing research modifies the perspective of the historian. Such achievement as the decipherment of Linear B and excavations at Knossos, Mycenae and Tiryns force him to the view that Greek culture was profoundly influenced by Egyptian and Mesopotamian civilizations. Whereas the development of mathematics and astronomy in the Hellenistic period leaned heavily on Babylonian science, biological thought, except for the concept of insanity, was derived from Egyptian medicine.

Dr. Saunders cites a number of specific examples of direct transmission of components of the Egyptian medical system into the Greek. These include drug and poison information, and several gynecological ideas which he traces from Egypt through Greece to medieval Europe In a more fundamental sense he points out, as does Sigerist, the previously unemphasized importance of rational and empiric elements in Egyptian medical theory. The separation of medicine from magic and religion took place at a very early period in Egypt.

A therory of pathogenesic involving decay of organic material present in excess, put refaction, and the liberation of a pyemic principle can be found in the medical papyri. These excesses, or residues, were to be found in the lower intestine and there the pyemic principle made direct entry into the vascular system because of the presumed intimate relation of large bowel to blood vessels. Thence the principle "rose" to other areas and produced disease. This "rising" is the counterpart of the Greek "flux", and the close relationship between Greek and Egyptian medical theory can be seen in this concept of pathogenesis. Although the classical humoral doctrine has received much more attention, it never displaced entirely the theory of putrefacive residues in Greek

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medical throught. The latter view persisted until as late as the time of Galen, who used it to explain febrile illnesses.

Dr. Saunders' argument is admittedly tentative because of the scant documentary material available. However, his analysis gives the reader an interesting view of an important sequence in medical history. The reliance on pure observation and the lack of experimental method that characterized ancient science made for the construction of scientific models in the form of analogies. However, analogies can be useful sources of newer and broader concepts of natural phenomena.

THE MANAGEMENT OF THE ANXIOUS PATIENT by Ainslie Meares, M.D., W. B. Saunders Company, Philadelphia, Pennsylvania, 1963, 493 pp. $9.00.

Reviewed by: LOUIS H. NAHUM

This book gives an account of how the author personally manages his anixious patient and the reasons for the various steps taken in this process. The author believes that a study of anxiety is the logical introduction to the whole of psychiatry and necessarily leads us to touch on other aspects of nervous illness. The general principles of Freudian psychopathology are accepted as causative factors. Nevertheless, the author believes that these influences are usually capable of satisfactory resolution without the interminable search for childhood and infantile conflicts.

The work is the outgrowth of the authors extensive experience and is based upon two cardinal assumptions. One is that there is a self regulating mechanism of the mind which he calls mental homeostasis. It is a transfer to the mind of the idea of bodily homeostasis which operates to help the physician and surgeon overcome disease processes in the body. When we administer an antibiotic or when a surgeon removes a disease process, the bodily healing mechanisms in the last analysis determine the patients recovery. A similar mechanism operates in the mind and the correct way to recruit the forces of mental homeostasis is to eliminate as far as possible the unsettling factors that cause anxiety.

The second assumption is that one way to help to restore the mental homeostasis is to allow the mind to regress to a state in which the intellectual and emotional disruptions that have upset homeostasis do not operate. He terms this state Atavistic Regression, and his experience has led him to believe that with this type of "rest," the homeostatic mechanisms of the mind will right themselves and anxiety will tend to disappear. The whole aim in his management of the anxious patient then is to facilitate the working of this mechanism.

When he considered the wide variety of methods of treatment of anxiety, from a religious experience, to non verbal communication, to hypnosis, to psychoanalysis, he had become impressed that atavistic regression was a feature common to all procedures that make the patient better and it was this insight that led to the formulaion of the atavistic theory of mental homeostasis. The mind, he thinks, does have self-adjusting mechanisms that restore homeostasis in the minor nervous aspects of every day living. He has seen some patients recover spontaneously as a result of some intrapsychic adjustment, while his environment remained substantially unchanged. In other cases, the author describes remissions as a result of lessening of external stress or because of some therapeutic experience in the patients life situation. He has seen dramatic improvements following analytic psychotherapy not because he thinks the patient learns to understand the underlying psychodynamic cause of his condition. Intellectual insight he finds therapeutically valueless, unless it is also accompanied by some kind of feeling or emotional experience. In short this method also works, when it does, by restoring mental homeostasis through atavistic regression.

The clinician of course, when confronted with an anxious patient has thus far derived little practical help from psychologic theory. The doctor does need a theoretical basis for his dealing with patients. The author believes that the atavistic theory provides a simple theoretical framework and a guiding principle which can clearly relate to all the doctor does in the management of the anxious patient. There is one basic guiding principle in practice: avoid alert critical conversation. We must behave with the patient in such a way that he finds it easy to let himself offguard and to regress. We must do this regardless of the therapeutic technique we are using. The good physician does this quite intuitively. He steers the anxious patient away from critical discussion. He allows him to relax in the security of his presence with very little verbal interchange. In short, the physician must always allow for concurrent atavistic regression regardless of the technique he employs with the anxious patient, whether it is conditioning, suggestion, insight and rapport.

This book is filled with a wealth of personal experience and much repetition, to bring home to the reader the two basic concepts; mental homeostasis and atavistic regression to help restore mental homeostasis. It is not meant for the psychiatrist or psychoanalyst who probably would need much more documentation than appears in this book before they would believe the thesis. It does offer a theoretical framework for the physician, student, social worker. It explains why many anxious patients get better if they are led to regress to a more primitive state of mind by establishing rapport thus leading him into a relaxed trusting relationship. Every doctor who wants to learn how to establish rapport with his patient can benefit from a careful reading of this book.

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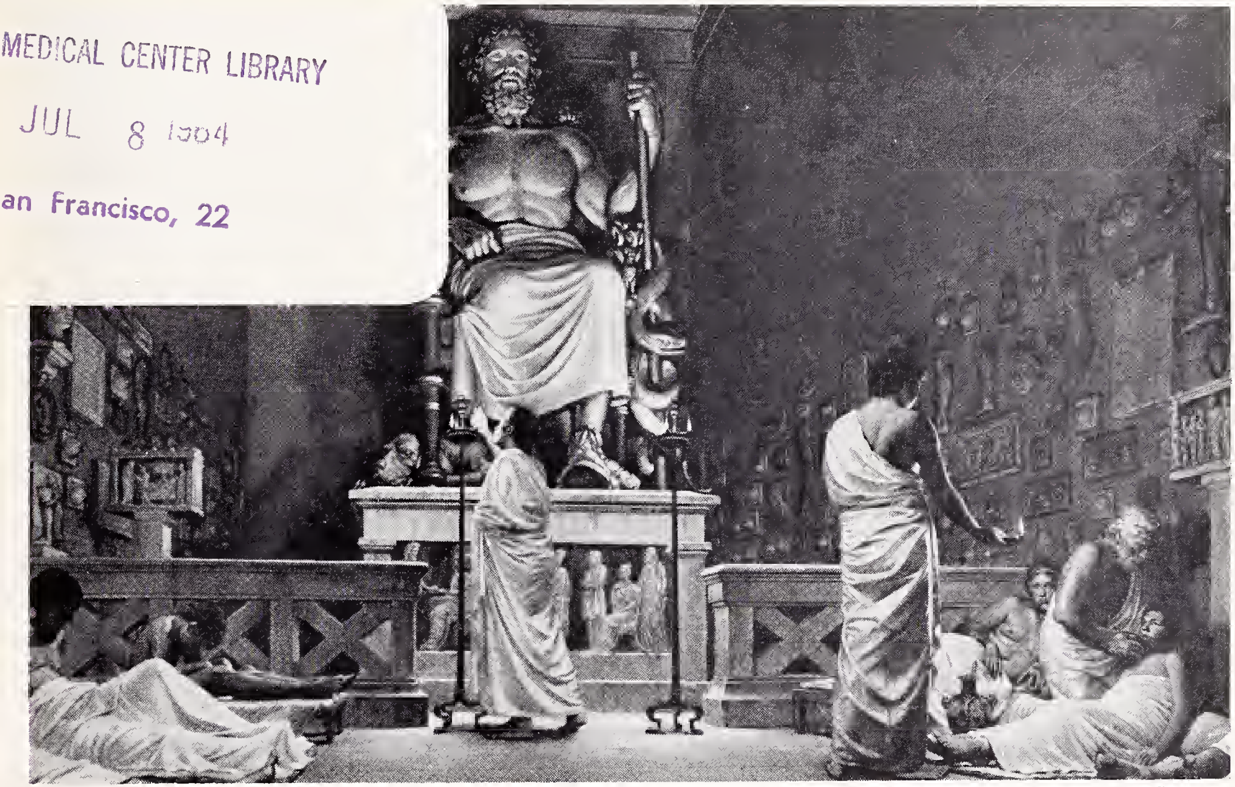

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THE TEMPLES AND CULTS OF ASCLEPIUS (see page 393)

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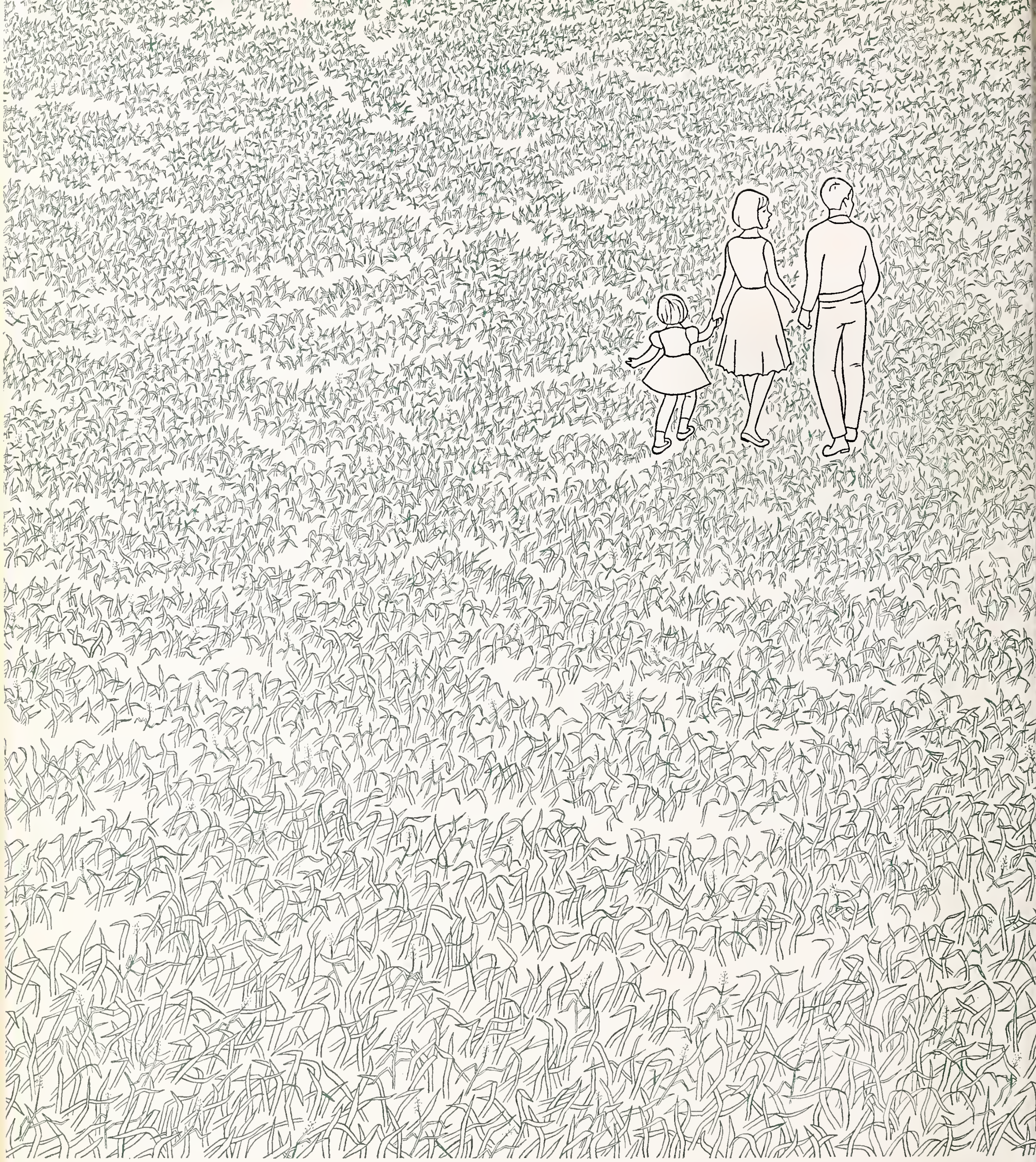

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editorials

A Short Review Of The Development of Pediatrics

Only lately has pediatrics been developed as a specialty. As a young physician, I saw its fight for independence. At that time there were very few professors of pediatrics. Pediatric teaching was in the hands of the internists. Only a few children's hospitals existed, and they were supported by private charity. Some infectious disease hospitals did exist, but general hospitals would not admit children under four years of age.

There were foundling asylums for newborn infants of unmarried mothers. These asylums were the cradle from which pediatrics originated. The foundling asylums did not keep the infants for more than a few days, as infectious diseases with a high mortality, were often found to develop. From the asylums the infants were placed in foster homes.

With the discovery of the small pox vaccination, the foundling asylums provided an excellent place for vaccinating the children. Each infant was vaccinated before it was discharged from the foundling asylum and it was here that it was discovered that the vaccine had a very mild effect upon new born infants; they had no fever, and the local reaction was mild. Vaccination of newborn infants has lately been revived.

It was due to the brilliant teaching of the pathologist, Rokitansky, that an important ruling was adopted in the Hospitals in Vienna which prescribed that every patient who died in the hospital had to be autopsied. The first scientific studies of newborn infants and of young infants following the newborn stage, consisted of the pathology of the gastrointestinal tract. Dr. Widerhofer, pediatrician of the Vienna University, explained that as long as the child was breast fed, it usually remained healthy. Gastrointestinal disorders started with the introduction of cow's milk into the infant's formula. Widerhofer described pathologic findings of these disorders as either catarralic or gastroenteritic, with or without ulceration. The ending "itis" meant inflammatory. Pathology could not entirely explain all of the clinical symptoms of acute and chronic diarrheic conditions. These symptoms could be better explained after the discovery of bacteria.

The leader in the field of bacteriology was Professor Escherich. The colon bacillus of Escherich is a commonly found bacterium of the gastrointestinal tract. Under normal conditions the duodenum is sterile. If the colon bacillus invades the duodenum, the gastrointestinal disorder starts. Milk has a long way to go from the cow to the child, and in the course of this can become infected. It is a good culture media for bacteria. The importance of milk hygiene, (boiling and clean handling) was, therefore, obvious. Professor Kassowitz felt strongly about this and would emphasize the fact that cow's milk would not be dangerous if it would flow from the breast of the mother.

The infectious childhood diseases initiated an intensive study to acquire knowledge concerning the causative agent and the mechanism of infections. A great many bacteria were discovered after the colon bacillus was detected, as for example, streptococcus, staphylococcus, tubercular bacillus, influenza bacillus, and of particular importance was the discovery of the diphtheria bacillus. Toxin and endotoxin were found to be responsible for clinical symptoms. Very soon thereafter, it was found that

THE COVER

THE TEMPLES AND CULTS OF ASCLEPIUS

EVERY NIGHT for nearly a thousand years (500 B.C.-500 A.D.) sick and afflicted pilgrims flocked to the Grecian Temples of Asclepius to take part in a ritual called incubation. The ancient, kindly god of medicine was expected to visit them during a dream-state and either heal them or prescribe drugs, diet, and modes of treatment. Only requisites were that they should be clean and "think pure thoughts." To show their appreciation, recipients of Asclepius' favor caused votives (stone or terra cotta images of the afflicted parts which supposedly had been healed) to be made, suitably inscribed, and presented to be hung as testimony on the temple walls.

antitoxin was neutralizing the toxin. The appearance of antitoxin in the serum demonstrated how nature healed the disease.

Experimental medicine developed a potent serum which proved effective in curing diphtheria. Later active immunization was developed and became improved by the use of toxoid. It was also extended to tetanus and whooping cough.

The use of serum disclosed to us knowledge of the serum sickness which in turn led to Pirquet's discovery of allergy. Serum disease and the discovery of allergy ushered in the tuberculin test and the diphtheria test. The discovery of the phenomena of allergy disclosed important new knowledge beyond pediatrics.

Meanwhile two great discoveries were made. The first was the discovery of the vitamins. Vitamin C against scurvy (Dr. Szent-György), and vitamin D against rickets. Other vitamins followed, named with other letters of the alphabet. The second great discovery was the introduction of the first antibiotic, a sulphor drug, followed by penicillin, discovered by Fleming. The antibiotic remedies started a whole new era in the treatment of disease, revolutionary in medicine.

Almost incredible to tell, there was among the antibiotics, streptomycin and isoniacin against tuberculosis. Dread tuberculous meningitis became a curable disease. Tubercular institutions closed down. The famous institution at Saranac shut its doors.

Scientists and physicians can be proud of their success and progress. Our advance in fighting against leukemia and malignant tumors has not been satisfactory. We have much to learn about virus diseases. Immunization against poliomyelitis and measles are close to complete solution. We have a great deal to do in the area of prevention of accidents which, unfortunately, are responsible for many deaths in childhood. We are hopeful for improvement in the neonatal period. We should make every effort to prevent prematurity. We cannot stand still. There is plenty left to be done.

Bela Schick, m.d.

A Trip To The Moon Or What's A Baby For?

Recently the question "What's a trip to the moon good for?" was parried with "Well, what's a baby for?" Questioner being questioned, the burden of reply was thus shifted back to the original proposer. So confounded, the second proposition was put in turn to many fathers and mothers, some of the replies are here recorded.

Caught un-prepared with "What's a baby for?" fathers responded in many moods. Plaintively: "To teach us that our lives are no longer our own." Belligerently: "What's a baby for? To be a parent later on, to populate the world, that's what for! Anything else you want to know?" Or quisically: "Is it a gag?" Then musingly: "Well, I want to raise a family of my own because I like a family. When I was a child I had a wonderful family." Architecturally: "A baby is to cement momma and poppa." Hopefully: "A baby to me is one who accepts and acknowledges warmth and recognition and will possibly provide for and look after me in my older days." Or genealogically: "If it's a boy it's to perpetuate the name of the father. It's the only kind of immortality that I believe in." Developmentally: "A baby gives me the satisfaction that I can handle more responsibility as though I were really grown up!" Egotistically: "To see the continuation of yourself in a child; the hope that what you haven't achieved in your life your baby can accomplish." Wistfully:" Makes you know what it's like to be a father and to be a son too. It helps you appreciate your parents more."

Mothers respond as a rule more directly and personally. "What's a baby for? For love!" or "Having a baby makes a better person of you. Once you have a child you learn the meaning of responsibility." "The satisfaction of being needed and wanted, this is important. It is gratifying to feel needed and wanted." Another replies glowingly "A baby gives you companionship. Life is not so lonely." Still another: "It is better than going out to play bridge." Humbly another replies: "Children are much smarter than we are, and you have to learn that it is possible to be smarter." Another observation: "It is possible to forget the harrowing hours of difficult labor because they were followed by such tenderness as the touch of my newborn child." Still another: "A baby can tell you what to do, can make you take orders and can run your life, and at the same time you can learn to behave and be tolerant." More vehemently: "A baby can drive one mad, and can give you a kindred understanding with people who beat their children to death!"

Replies reflect a multitude of viewpoints apparently too heterogeneous to yield a common denominator. Perhaps the answers reflect only the problems and needs of the individuals. If, on the other hand, for the question "What's a baby for?" the reposte is "What's a child for?" and this in turn is parried with "What's a man for?" One can begin to see the woods despite the trees. The baby, the child, the man are all parts of the same question. At whatever stage, they are always the individuals who make up the long line that carries the thread of life, with all its implications, from generation to generation. Perhaps this is the answer to "What's a baby for?" A baby is our future, all of our hopes,

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prayers, our fears, our tears; to carry the thread of life over the horizon into the future. That's what a baby is for!

VICTOR L. SZANTON, M.D.
Guest Editor.

Stork Duty* Babies

By times, babies are born at the roadside, in cars, in restrooms, busses, trains and in other impromptu settings. Newspaper reports frequently begin "The proverbial stork won the race to the hospital last night" and go on to say that mother and child are doing nicely. So far so good.

On arrival at the hospital the dilemma begins: The newborn child is considered potentially infected and is not eligible for the newborn nursery. In many hospitals the baby is placed in a "suspected of infection" nursery, but more often in a pediatric ward. The mother, similarly, is sometimes "isolated" on the maternity ward, but more often bedded down in a medical or surgical ward. As patients, both are exposed, needlessly, to the infective atmosphere of the hospital areas.

There are preferable ways of handling this type of situation. If no contraindication exists, it might be feasible to return mother and infant home for convalescence. A better procedure would be for both to be together in a room, at the hospital, kept aside for such isolation purposes. Realistic arrangements could be made for their nursing care during their hospital stay. This would not be in conflict with the sanitary code or with acceptable hospital practice.

We who are hospital administrators, nursing supervisors, chiefs of obstetrics, directors of pediatrics and admitting office physicians have been able to provide and encourage the use of post operative recovery rooms, intensive care and self care units. Can we not now bring the pediatric care of the "stork duty" babies up to date?

V. L. S.

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* The euphemism applied to amateur obstetrical services rendered by policemen, firemen, civilian defense workers, etc.

The Shoemaker's Children

"Doctor's children get the darndest ailments" has been said endlessly as though it were folklore or superstition rather than reality. The reality is that this is the hazard of being a doctor's child. Physician-parents are rarely willing or even able to give recognition to the medical needs of their children because of their distracted focus of attention. Instead of being impelled, as most parents are, to obtaining advice for their child, their attention is fixed upon their own feelings of inadequacy, their emotional involvement, and their embarrassment at having to "bother" a colleague for medical services. The doctor's child lives under this threat as well as the jeopardy of the parent's occupation since doctors, because of their occupational exposure, are frequent carriers of viral and bacterial flora. The doctor's child then, who probably needs more medical attention than the usual child, actually gets less. Because of this, it follows that the attending physician or pediatrician carries a greater burden than the situation normally requires.

This point is very well made by Drs. J. H. Kennell and Willard B. Boaz (Ped. Vol. 30 July 1962 pp. 100-108). The ground rules for the attending physician and the parent physician are well worth repeating.

"1. Early contact with the family.

Doctor parents should be encouraged to make definite arrangements for the attending physicians' services and to meet with him before the birth of their baby, or as soon as they move to a new location.

2. Talk with both father and mother.

It will be profitable for the attending physician if he will set aside time to present his plan of medical supervision to both parents, together whenever possible.

3. Anticipate the father's concern about calling the attending physician.

The attending physician may say that:

a. despite the fact that he is busy, he wants to be telephoned at the beginning of an illness or whenever the parents have concerns or questions.
b. He will not resent calls even for something that may prove insignificant.
c. From now on he considers that their child or children are his patients, and that he will feel he has been used unwisely if he is not consulted on all matters pertaining to the childs health and illnesses.

4. The attending physician is the only doctor.

The attending physician should stress that he must assume medical responsibility. The doctor-father (or mother) has only the parental responsibility for this child. The attending physician must be alert to violations of this arrangement and correct them promptly.

5. Stress interest in health supervision.

The attending physician can make it clear that he wants to see the child regularly whether he is sick or well, whether he needs immunization or not, so that he can guide the parents with his overall management.

6. Talk with him before consulting a specialist.

It is much easier to talk about touchy matters such as self-referral to a specialist at the first meeting with the parents than after this has actually happened. The attending physician can indicate that it is essential for the parents to discuss the need for referral to a specialist with him before any decision is made, if he is really to be effective in the comprehensive supervision of their youngster's health. At this time he can tell them how difficult it is for him to be frank with a doctor's family after they have already made an appointment with a specialist or have received his advice.

7. Discuss the "Medical Superstition."

The attending physician has an excellent opportunity at this introductory meeting to express why he believes that physician's families have more medical complications than others and to explain that this should not happen to them if they follow the suggestions he is making.

8. Discuss the increased concerns of the physician's family.

During the initial appointment it is helpful if the parents are told that their medical background may make child rearing more difficult for them than for other parents, because of the many pathological conditions that will occur to them as they care for their youngster. The attending physician will also be wise to point out how the narrowness of specialty training and experience may distort the parents' view of their child whether he is sick of well. He can use this phenomena and the many anxieties arising from a medical background, as reasons for consulting him as much or more than other parents. The pediatrician will want to make clear his plan to take care of their child just as he does other children. This will include a full history, with details of child rearing and family policies.

9. Mention the possibility of dissatisfaction.

The attending physician is wise to tell the family that they might want to switch to another doctor sometime in the future. He can point out that the personality and methods of one doctor are never compatible with all patients. Then the family will find it easier to speak out about their dissatisfactions to him if these ever develop. By bringing up the subject in the beginning he indicates this is to be expected occasionally and will not surprise him or anger him.

10. The attending physician should keep full medical responsibility.

The attending physician should not ask the father to do painful or disturbing procedures on his own children, such as giving a "shot" or taking a culture. He must not push responsibility back on the doctor-father by asking him to check ear drums or a throat.

11. Suggest that the mother call the pediatrician.

The attending physician may recommend to the mother and father that it is standard procedure for the mother to take the initiative in calling the physician whenever she has a question about illness or health, like the overwhelming majority of other American mothers rather than ask her husband's advice or permission first.

12. This simple method will automatically eliminate the two greatest sources of difficulty: the father's fear of imposing and the father's overconcern due to his own specialty. If the father is not responsible for calls, he does not have to feel guilty about them.

Management During Illness

1. Avoid exceptions.

When the doctor's child develops a problem the attending physician should give him the same advice and treatment that he provides for other children. He should use the same medicine, write out prescriptions in the same way, and set up the same plan for follow-up examinations. The child of a doctor should be able to obtain the same quality of medical care that is available for all other children. It is just those deviations from routine medical care made out of deference to a professional colleague that so often lead to complications in the family of a doctor. It is suggested that one simple solution will answer all the questions raised about the management of a doctor's family: treat the doctor's family like all other families.

2. When a parent shows disproportionate concern:

The experienced physician has an added reason to assume complete medical authority if one or both of the parents show anxiety beyond what would seem appropriate for the illness, as with any other family. If thorough study, diagnosis and adequate treatment of the patient do not lead to a lessening of the parent's concern, a pertinent discussion with the parent is in order. Such a talk should be conducted while seated, removed from the patient, with adequate time to allow the anxious parent opportunity to express the underlying worry. Often this anxiety will stem from a case in the doctor-father's own practice or from his professional reading or from an unpleasant experience in his own past history. Usually the open discussion of a half-suppressed worry will make it very evident that the child's situation is quite different from the one in the parent's mind and will bring about a dramatic relief, to the benefit of the patient as well as the parent.

The experienced physician will realize that the problems presented have no easy solution. To handle them optimally he knows he must establish a mutual confidence with his patient and family over a period of time. He will not expect results

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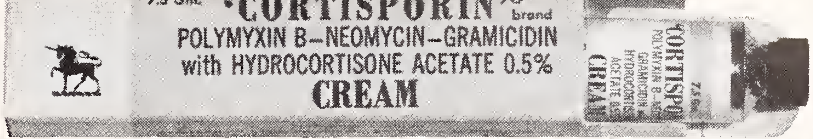
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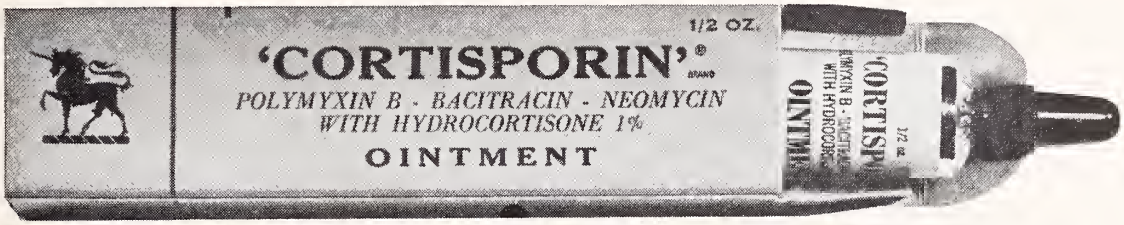

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from such short cuts as handing the father or mother this report."

That the shoemaker's children do not have shoes should not imply that a doctor's child should not have appropriate medical care.

V.L.S.

"Natural Childbirth" vs. Use Of Drugs During Labor

Moya and Thorndike[1] have reviewed the effects of drugs used in labor on the fetus and the newborn. Data from experimental animal studies and human clinical investigation indicate that "the newborn shows marked susceptibility to the depressant effects of drugs used in labor. This heightened sensitivity is related in part to increased permeability of the blood brain barrier, inefficient metabolism and asphyxia, and physical trauma associated with the delivery process. The human studies were limited by the fact that the neonate was evaluated by what can be observed in the delivery room. The question, however, remains whether the effect of drugs given to the mother persist beyond the immediate delivery and for how long. An answer to this question might yield information not only concerning our understanding of the drug action on the neonate, but also the quality of the organization of a newborn's behavior.

Stechler has just published his results on newborn attention as affected by medication during labor.[2] He presented 3 stimuli to an infant, a face, a few dots and a blank, and studied the visual fixation of 20 full-term babies from 2-4 days old from normal deliveries and with no gross pathology. Earlier than two days visual testing is impaired because of eyelid swelling from silver nitrate administered at delivery. The total time spent staring or scanning the stimulus area was contrasted with total of the range of non-attentive behavior such as looking away, closing eyes or fussing. The author did not have information on the medication of the mothers at the time of the visual testing and therefore was not biased in the evaluation of the attentiveness of the baby.

The major drugs studied were meperidine, alphaprodine, pentobarbital and promethazine, all are depressants and act in the same direction although not on the same centers of the nervous system. The first three of the group act relatively rapidly with peak action time of less than 1½ hours. Stechler found that there is a significant relationship between the administration of certain drugs used in labor and the attentiveness of the infant. The results were not related to the sex of the infant, the birth weight, the length of labor, to the gestational age (all were full-term normal infants) or to age (between 2 and 4½ days). The stimuli themselves have a marked effect on the duration of visual attentiveness which they elicit. Out of 180 sec. of exposure for each stimulus the average attention toward *the face* is 105 sec., while for the dots and blank the average was 88 and 42 sec., respectively. The mean total looking time for the group having had the drug within 1½ hours, was 195 sec., while for the control group the mean was 287 sec. If the mother received more drugs closer to delivery, then the infant was even less attentive. Thus there was found a significant relationship between administration of depressant drugs used in labor and the attentiveness of infants 2 to 4½ days later.

There was an erroneous view that the infant has little or no pattern vision during the early weeks or even months because of the need for usual learning or because of the immature state of the eye and brain. Fantz,[3] however, produced evidence that during not only the early months but the first 5 days of life, infants have fairly acute pattern vision and show greater visual interest in patterns than in plain colors, differentiate among patterns of similar complexity and show visual interest in a pattern similar to that of the human face. In the 18 infants under 5 days of age Fantz found that they had an innate ability to perceive form, exhibiting twice as much visual attention to patterns as to plainly colored surfaces. Stechler's study successfully used Fantz's method to confirm his findings and to demonstrate further that depressant drugs adminstered to the mother within 1½ hours of delivery produce a long acting effect on the infant reducing his visual attentiveness.

A central question which remains unanswered is the persistence of the effect beyond the age of 4½ days. Nevertheless the persistence of some drug influence in the neonate for so much longer than in the adult, supports the concept of greater vulnerability in the immature organism to depressant drug. On the basis of Stechler's studies one can certainly make out a strong case against drugs and in favor of "natural childbirth."

L. H. N.

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Mental Retardation And Asphyxia Of The Fetus

Until recently we did not know to what extent permanent brain damage may result from anoxia or asphyxia during parturition although there have been hundreds of speculative commentaries written on this topic. Windle's experiments on Rhesus monkeys have at last brought some understanding in this admittedly confused field. It is confused because many factors can enter into the final result of mental retardation, such as asphyxia, an accompanying acidosis, birth traumata, prolonged labor with increased intrauterine pressure and contractions, and kernicterus with and without asphyxia.

The rhesus monkeys have menstrual cycles of about 28 to 30 days, almost identical with those of women. They breed freely in all seasons and most conceive when mated on day 11 of the cycle. Placentation is similar with that of women but gestation shorter, lasting six months and the offspring is a little more advanced than the human infant. It seems reasonable that it should be possible to transfer the experimental data from the monkey to the human being, certainly more reasonable than from the guinea pig to the human being. The rhesus monkey is also an excellent animal to study factors in the genesis of mental retardation, because it is easy to produce brain damage by asphyxia experimentally and one can be sure of the results because mental retardation is almost never encountered spontaneously in this experimental animal. Although it is easy to separate all factors and control the experiment in animals, in humans the effects of asphyxia cannot be separated clearly from those of anesthetics and other drugs used in obstetrics

Windle found, that, when asphyxia lasting six minutes or less was induced animals continued to breath and their brains showed no neuropathology. However, if the period of asphyxia lasted seven to nine minutes, the animals required no resuscitation but the brains showed discrete lesions in the thalamus and inferior caliculus. It is difficult to know why with, brain lesions, the animals showed no mental retardation. Perhaps the psychological tests Windle used were not sufficiently refined to reveal effects of relatively minor changes limited to the basal ganglia.

If the animals were asphyxiated long enough to require resuscitation, then a constant pattern of nervous system damage was found in all monkeys and the severity of the damage was roughly proportional to the duration of asphyxia. In the brain stem, sensory systems are more severely affected than other systems, whereas motor nuclei and visual systems were spared. As time went on scars formed. The animals were hypoactive, sometimes ataxic, unemotional, awkward and aphonic. They couldn't suck, right themselves, and feeding was a great chore. It was not possible to establish the point in time during or after an episode of birth asphyxia when the neural damage became irreversible.

After separation of the placenta and the fetus can no longer obtain oxygen, then the central nervous system is affected by acidosis as well as oxygen lack and by depletion of carbohydrate reserves. Under these conditions nerve cells are damaged and some die. But not all parts of the brain are equally affected. Perhaps some parts use oxygen more rapidly than others. Apparently the sensory systems are more severely affected than the motor systems. It would seem that if oxygen per se kills the nerve cells then there would not be much hope of therapy and one can then only strive to avoid asphyxia during birth. However it could be that an associated acidois and depletion of carbohydrate stores also play a part since it is known that the fuel of the brain is glucose. By giving alkali to prevent the blood pH from falling and at the same time supplying carbohydrate during and after asphyxia episodes, Windle found that the survival rate would be significantly increased.

Some monkeys asphyxiated for 15 to 16 minutes at birth and resuscitated survived. They showed symmetrical diencephalic and brain stem lesions and sometimes also neocortical and cerebellar as well. Counterparts of these lesions have been found in the human brain also. The monkeys developed marked neurological defects often closely resembling a human being with cerebral palsey.

Windle points out that he has been able to obtain mental retardation in monkeys from conditions other than asphyxia neonatorum, but then, the animals showed a different type of neuropathology. When he gave oxytocin near the end of gestation to induce labor, strong uterine contractions occurred and the intrauterine pressure also rose. The fetuses did not die but one showed cerebral hemorrhage. The animals were depressed at birth and during the post partum period. They did not show the same lesions described during asphyxia but marked bilateral atrophy of the post central gyri of the cerebrum. Since the asphyxia during birth was not complete, some other factors must have come into play.

The new born baby has a much larger head than that of the monkey infant. It is therefore possible that traumatic hemorrhages may be more prevalent in human babies than in the new born monkey, but we do not know to what extent cerebral hemorrhages at birth are responsible for mental retardation. However, Windle was able to experimentally produce traumatic deliveries in monkeys by the breech method of presentation and produce mental retardation in the offspring. In this case the lesions were different than those caused by asphyxia.

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
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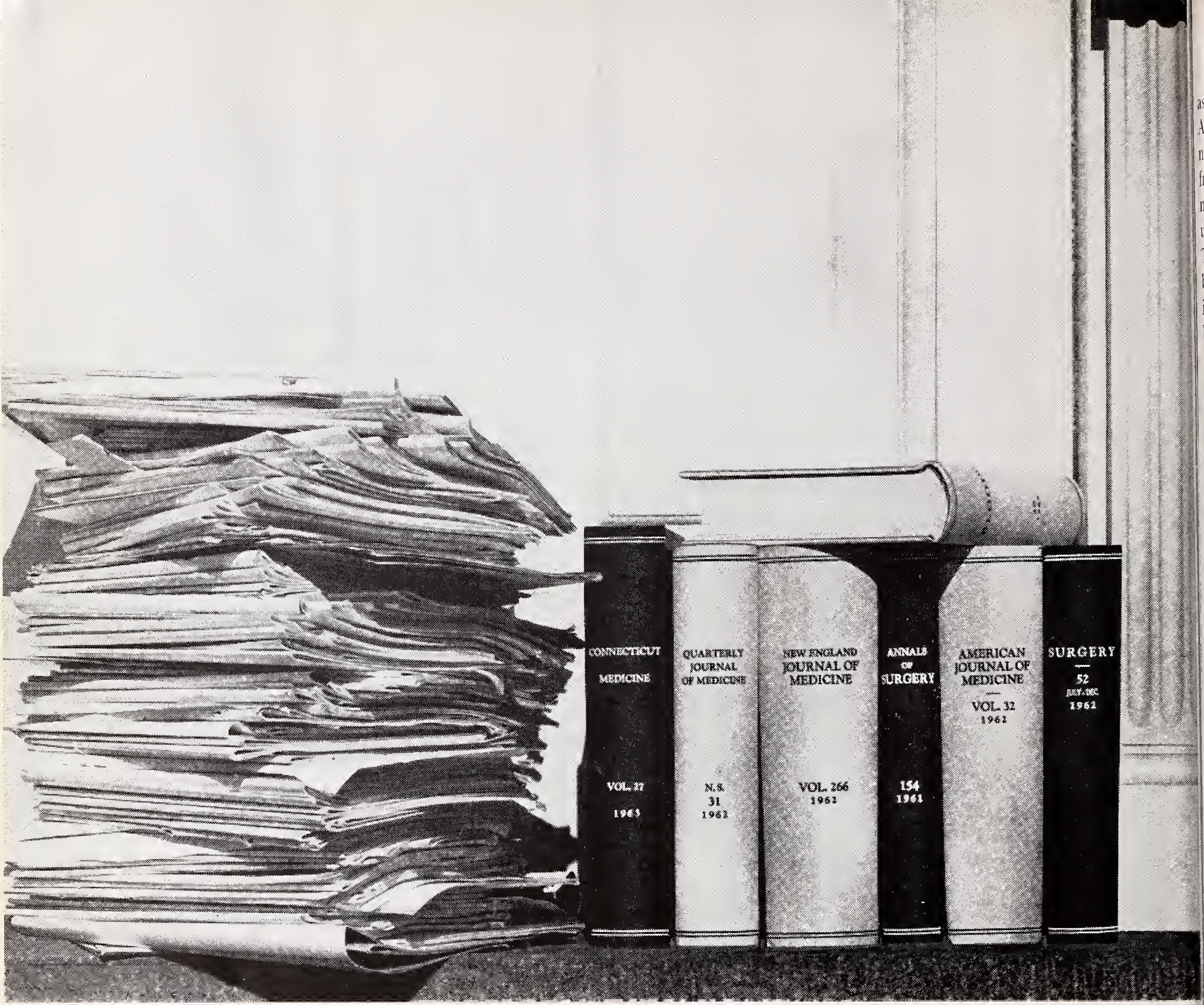
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In human infants mental retardation is at times associated with hyperbilirubinemia and kernicterus. Apparently they develop selective bile salt impregnation of neural tissue when the infant has suffered from erythroblastosis fetalis. Windle however could not produce mental retardation in his animals unless he combined this with an asphyxial episode. Then the pigment from the blood passed into the brain tissue and neuroglia similar to what is found in the human infant, and the kernicterus monkeys became unquestionably retarded.

These experiments on monkeys illustrate the probable mechanisms of brain damage in human infants. They do not deal with forms of behavioral and intellectual impairment that are related solely to socio-environmenal factors. They do reveal that the grade of asphyxia is crucial in development of mental retardation, that acidosis and disappearance of carbohydrate stores are contributing factors and that trauma also plays a role in damaging the central nervous system. The lesson to the physician from these experiments is obvious.

L. H. N.

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Critical Periods Of Early Stimulation

If rats are handled during the first ten days of life, such stimulation produces an animal that is more vigorous, learns more quickly and is less timorous. Levine[1] found that not only handling, but a variety of other stimuli such as electric shock or mechanical shaking will accomplish the same thing. Obviously this ruled out learned behavior as an explanation of the effect. What else could it be due to?

It had been known for some time that laboratory rats are quite deficient in adrenocortical response as compared to the wild variety. Then Levine *et al* discovered that animals handled in the early period showed a much earlier maturation of the adrenocortical response to stress. Levine interpreted these results as indicating that the laboratory environment did not provide sufficient stimulation for the proper development of the hormonal system of animals. The adrenal response in any case matures and becomes fixed by sixteen days of age. If the hormonal mechanism is the chief phenomenon involved, then the critical period for optimum development of the adrenocortical stress mechanism must occur prior to sixteen days of age. According to Thompson and Schaefer[2] the critical period is really the first week or ten days.

The question remains whether the level of stimulation is important as well as the time of its application. It is conceivable that either very weak or very strong stimulation might produce poor results, so that there might be different critical periods for the effects of early stimulation depending upon the intensity of early stimulation and the kinds of later behavior measured. With this hypothesis Denenberg[3] investigated the critical first ten days. He found that the best avoidance learning was produced by stimulation in the second half of the period. Whereas, the best survival rates were produced by stimulation in the first half. Unhandled controls performed poorly because they were too emotional. The rats that were handled too long, that is, for the first twenty days, also performed poorly because they were too calm to react quickly. The best results therefore, were obtained from handling only in the first ten days of life. In short, no handling produced too much emotionality and too long handling resulted in too little emotionality.

Irrespective of the effect on learning, Denenberg's data lead to the important conclusion that emotional stimulation during a critical period in early life can lead to the reduction of emotional responses in later life. Apparently there appear to be two critical periods that are revealed by early stimulation of rats. One is based on physiologic process, the development of the adrenocortical stress mechanism which can be speeded up by early stimulation. The other is based on a psychological process, the reduction of fear through familiarity beginning about seventeen days when the eyes first open and extending to thirty days. The extent of handling during these two periods are additive. In short, the significant experiments are those based on the developmental period rather than arbitrarily on them.

Clearly, this knowledge of critical periods of stimulation in rats should direct our attention to whether similar periods exist in the human infant. Two kinds of studies are in process to determine whether similar factors operate in the human infant. One type deals with reactions of infants when separated from their mothers, and the other is to stimulate emotional responses in mothers and observe the effect on the offspring.

In the first type of study Bowlby[4] found that a large proportion of juvenile thieves had been separated from their mothers in early infancy. He postulated on the basis of this retrospective study, that such traumatic emotional experience had affected their later behavior. This led him to study the primary symptoms of separation. He described in detail the emotional reactions of infants sent to hospitals and thus separated from their mothers.

Schaeffer[5] found a difference in reaction to separation before seven months and separation afterwards. Both sets of infants were disturbed but they were disturbed in different ways. Infants adopted from three to twelve months of age show increasingly severe emotional reactions. Apparently the critical period for maximum emotional disturbance is approximately seven months, which is the end of the critical period of socialization. Infants in which social relationships and responses have not yet been established are less likely to be upset by changes, than older infants whose social relationships have been thoroughly established and whose fear responses towards strangers have been fully developed.

Scott[6] points out that not all apparently traumatic early experiences have such a lasting effect. Experimental animals have a considerable capacity to recover from unpleasant emotions experienced in a limited period in early life. What is traumatic in one species may not be so in another. He also emphasizes that critical periods are not necessarily involved in every kind of early experience. Here then is a fertile field for investigation.

What happens to an offspring when emotional responses have been produced in the mother? Thompson[7] has shown that the offspring of rats made fearful while pregnant are more likely to be overemotional than the offspring of animals not so stimulated. To eliminate the factor of influence on maternal behavior, the offspring were brought up with foster parents. It therefore, seemed likely from what has been said above that the result was produced by modification of the adrenocortical stress mechanism, in this case by secretion of maternal hormones acting on the embryo rather than by stimulation after birth of the young animal itself. No precise critical period for the effect has been established but it is probably confined to the latter part of pregnancy. Similar effects have been obtained in mice and if such effects can be demonstrated in other mammals, the implications for prenatal care in human beings is obvious.

Scott brings the subject into clear focus as follows "Both growth and behavioral differences are based on organizing processes. This suggests a general principle of organization. Once a system becomes organized whether it is the cells of the embryo that are multiplying and differentiating or the behavior patterns of a young animal that are becoming organized through learning, it becomes progressively difficult to reorganize the system." Clearly the time for further organization to be strongly modified is only when active processes of organization are going on. These are the "critical periods of behavioral development." These we must learn to know, master and manipulate for the benefit of animals and man.

L. H. N.

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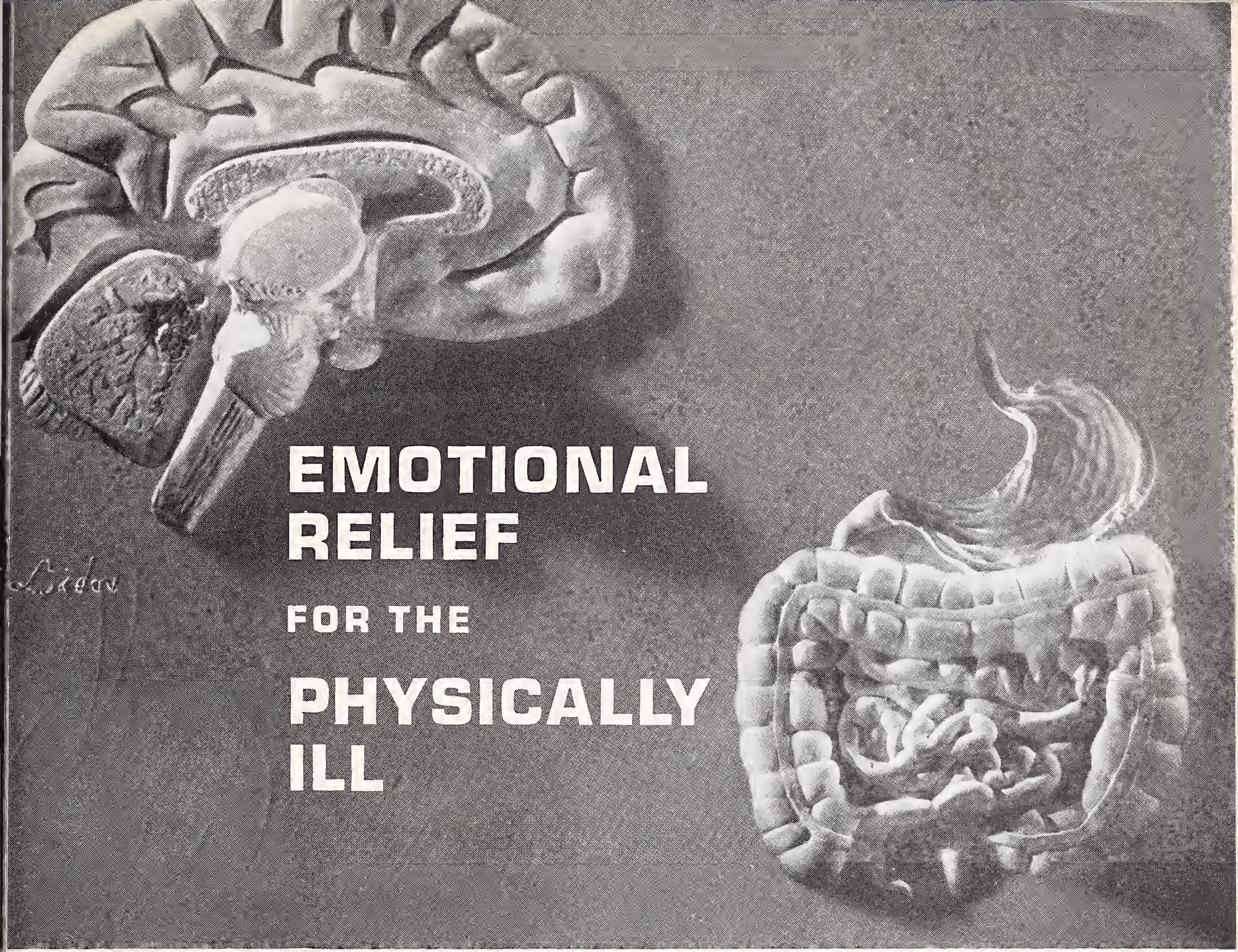
Exterogestation

Man is born and remains immature for a longer period than any other animal. A new born elephant and the fallow deer can run with the herd shortly after they are born. At the age of six weeks the infant seal taught by his mother can navigate his watery world for himself. Obviously the human infant arrives long before he becomes ready to face his world by himself.

Ashley Montague in a recent paper[1] proposes the hypothesis that this is to be attributed to the great increase in the size of the infant's brain and his head, as compared to other animals so that if the human infant were not born when he is, he wouldn't be born at all. At birth the average brain volume is 350 cc. If this were increased slightly, the head could never pass through the birth canal, as in fact it sometimes doesn't. It follows that the head must continue to grow outside the womb. Stated in another way, the survival of the fetus and mother requires termination of the gestation within the womb (interogestation) long before maturation occurs, and at a time when the head size is still compatible with birth. The remaining part of gestation that is not completed within the womb must occur outside and is termed exterogestaton.[2]

The average duration of exterogestation is arbitrarily considered to be at the stage of development of effective locomotion on all fours. Interestingly enough it is about as long as interogestation and also about as long a time as the mother formerly used to nurse her infant. It is a period also during which, generally, pregnancy will not occur. This hypothesis then states that man spends half of his



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gestation period within the womb and half outside the womb.

During the first year when the infant has so much to learn, the brain growth is the greatest from 350 cc. at birth to 800 cc. At three years it is 1,250 cc. In adult life it is 1,450 cc. It is clear that such maturation as other mammals complete before birth, the human animal by virtue of the size of brain needed to function, must leave the gestation period extended beyond birth. In some mammals like the marsupial's, the little immaturely born infant is born into its mother's pouch, there to undergo its exterogestation until it is sufficiently mature. Although the human infant remains immature much longer than the infant kangeroo or opossum it is afforded no such natural advantage.

The exterogestation hypothesis holds that the biological unity, the symbiotic relationship existing between mother and fetus throughout pregnancy does not cease at birth, but is naturally designed to continue after birth and perhaps more so. After birth not only the infant has a great need of continuing support from its mother, but the mother has an equally great need to continue to support and give succor to the child. Montague points out that the mother's interest is deepened and reinforced in the child's welfare and that her whole organism "has been readied to minister to its needs to nurse it at the breast." The continued symbiotic relationship between mother and child confer upon each psychobiological benefits which are vitally important for the future development of both.

The hypothesis of interogestation and exterogestation proposed by Montague may, if taken seriously by pediatricians and others lead to a reconsideration of the meaning of the human infant's dependency and immaturity. Just when the mother and child need each other the most, they are too often separated from each other. Viewed in this light it cannot be considered an advance when a bottle formula is substituted for the product of the human breast, or when the mother and child are banished from each other by installing a crib in a nursery. Long ago and before the exterogestation hypothesis was conceived, psychologists had been seriously studying the influence of mother upon infant during the first months and years of its life. Perhaps pediatricians will now take up the challenge of this hypothesis, and reevaluate the substitution of bottle for breast, and a nursery, where no nursing takes place, for the mother.

L. H. N.

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Mental Effect On Pregnancy Being Studied

The theory that the attitude of an expectant mother toward pregnancy can affect the course of the pregnancy is being studied by researchers at Mount Sinai Hospital New York City.

A self-rating attitude test is being given to expectant mothers during the early months of pregnancy, Abram Blau, M.D., Joan Welkowitz, Ph.D., and Jacob Cohen, Ph.D., reported in the current *Archives of General Psychiatry*, published by the American Medical Association.

The scores will be analyzed in light of the subsequent course of the pregnancy.

The test was devised as a possible method of predicting probable premature births and other complications of pregnancy due to psychological factors, according to the researchers.

It consists of 48 statements to which the examinee can agree, strongly agree, disagree, or strongly disagree. The items focus on attitudes and apprehension regarding the mother's ability to carry the unborn child to term; anxious anticipation, ambivalence or negative feelings, regarding the health of the coming baby; negative feelings, depression, fatigue, and nausea during pregnancy; and attitudes toward breast feeding.

"We anticipate that some significant relations with obstetrical abnormalities will be demonstrated," the researchers commented.

"If corroborated, a simple test of some predictive utility for psychogenic obstetrical complications may evolve."

Preventive measures could be taken if complications were expected, the authors pointed out.

There is a general belief that psychological factors influence motherhood in terms of sterility, spontaneous abortion, premature terminations, and complications of delivery, according to the authors. However, research into these factors has been limited, they said.

In a previous study, Dr. Blau found that 30 women who delivered prematurely in the absence of any accountable medical factor differed from a similar group of 30 women who delivered full-term infants. The premature group showed negative attitudes to the pregnancy, greater emotional immaturity, greater concern about physical appearance, and less adequate resolution of family problems.

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■ The Connecticut State Department of Health is responsible for licensing of hospital maternity units. This is part of the state department of health's general hospital licensing program, and is assigned to the maternal and child health section to carry out. Discussion of this activity, which is part of the broad field of maternal and child health, was selected as representing one way in which the state department of health carries out its responsibility for the promotion of the health of mothers, children and families in Connecticut.

Prior to 1937, maternity units of general hospitals were licensed by local directors of health. The original regulation implementing statutory responsibility as well as the subsequent revisions was the result of the joint effort of the Committee on Public Health of the Connecticut State Medical Society and the Connecticut State Department of Health. As the Committee on Public Health took on increased responsibilities, a Committee on Maternal Morbidity and Mortality was established to work specifically on problems associated with maternity. When this committee was formed, it, therefore, was involved in revisions of Regulation 202, Public Health Code of Connecticut.

Regulation 202 of the Public Health Code indicates the minimum requirements to be met by maternity units.[1] Connecticut hospitals, however, go beyond minimum requirements and work toward reaching standards according to those recommended by groups such as the American Academy of Pediatrics,[2a,b] American College of Obstetricians and Gynecologists,[3] American Hospital Association,[4a,b,c] the U.S. Public Health Service,[5a,b,c] and others.[6a,b,c,d,e,f] In addition, there are standards on specific situations developed by Connecticut State Department of Health and the Connecticut State Medical Society.[7a,b,c]

The Licensing-Consultation Visit

Maternity licensing and consultation functions require a number of consultants. A physician and public health nursing consultant make the hospital visits, accompanied at times by an epidemiologist, sanitary engineer, research microbiologist, and others, as appropriate. Recommendations and findings of these visits may then be reviewed with members of the "extended team" which includes the chief of the maternal and child health section, a social consultant, nutritionist and statistician. Staff from other sections of the department, including laboratory, preventable disease, hospitals and sanitary engineering also work with the maternal and child health staff as the need arises.

Though licensing connotes inspection, the visits are actually a consultation service. Usually there are joint conferences with members of the hospital staff relative to changing trends in medical and nursing care of maternity patients and newborn. The joint meeting by physicians, nurses and administrators may be one of the few times that such an interdisciplinary hospital group meets at a number of hospitals. The success of such discussions would lead one to hope that a similar pattern could be developed through which maternity and newborn services are evaluated and improvements in hospital care made.

At these conferences the state health department staff bring to the hospital staff ideas learned from other hospitals, and, in turn, subsequently shares with the other hospitals that which was found to have been of value to the hospital being visited. For example, one of the most spectacular of the new trends that have been going on has been the number of variety of disposable items available for use with hospitalized mothers and babies. The list is endless, but some of the more popular items are disposable exchange transfusion sets; disposable gloves for rectal and vaginal examinations; disposable enema sets; disposable catheterization trays; disposable infant nursers, and disposable footprinting pads. As one hospital gains experience, we can refer to that hospital as a resource for another hospital that may express an interest in trying out a new procedure, a new technique, or a new method of care.

SPECIAL VISITS

Special visits are made at the request of the hospital administrator, chief of the obstetric or newborn services, director of nursing, maternity supervisor, or chief of pathology. The kinds of requests that have been received for special visits have to do with such items as construction or reconstruction in maternity units, admission policies,

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DR. LOUIS SPEKTER is former Chief of the Maternal and Child Health Section of the Connecticut State Department of Health.

prevention and control of infection, and nursing procedures. Special visits are also made when the maternal and child health staff sees the need for a follow-up visit as a result of previous visits, on reports of outbreak of infection and for inspection of facilities about to be used for the first time.

USE OF STATISTICS IN HOSPITAL CONSULTATION

Neonatal mortality rates were used as a measure of hospital care for many years. There was a weakness inherent in depending on a single measure since it did not give sufficient information. Moreover, there was also a weakness inherent in using neonatal mortality rates alone due to over-reporting or under-reporting of fetal deaths.

To obtain a more accurate picture, perinatal data for each Connecticut hospital was calculated in 1961 for the three-year period of 1957-1959. In addition, perinatal mortality rates were obtained by race and by weight in 500 gram increments. The material was published in 1963.[8] During 1962 the maternal and child health staff met with staffs of hospitals whose perinatal mortality rates deviated significantly from the Connecticut average to see whether some of the factors associated with this deviation could be defined. Hospitals with a better than average record are as much of interest to us as hospitals with a less favorable record. It seemed as important to learn of the factors that appear to be associated with a good perinatal mortality record as it was to learn of those that might be expected to lead to a high rate.

Certain factors influencing perinatal mortality may not wholly or partly be influenced by hospital practices, viz., socio-economic status of maternity patients; the lack of understanding for health services; availability of health services. These factors should be noted, of course, and community action taken to correct these deficiencies. One would, however, look directly to the hospital staff for certain policies and activities that would tend to improve the perinatal mortality record, as for example:

> An active hospital perinatal mortality committee which periodically reviews the deaths and makes recommendations for improved hospital practices; an interested and informed medical and nursing staff; nursing staffing adequate in number, and responsibilities and duties of nurses appropriately and specifically defined; an anesthesiologist available to administer anesthesia to the mother and to resuscitate the newborn; good prenatal care for both clinic and private patients as a concern of the medical staff; interest in referral to community agencies, including public health nursing as well as social agencies, of selected families who could benefit from this.

Hospital Studies

1. One hospital was faced with an unusual situation in that many contributing factors were present which one might expect to result in a low perinatal mortality rate. In spite of this, it had a higher than the Connecticut average perinatal mortality rate. After exploration as to how one might study the non-hospital factors involved in perinatal mortality, the hospital staff decided they would study the social, economic, educational and cultural aspects of the families who contributed to the hospital's perinatal mortality.[9]

Data was accumulated from current hospital records and from interviews with patients who were admitted to the maternity unit for a six-month period in late 1962 and early 1963. Even though a small number of patients was involved, approximately 500, there appeared to be an inverse relationship between family income and perinatal mortality.

This finding indicated a need for a more extensive utilization of community services to improve the chance of certain mothers having healthy babies. It was found that many families with low incomes had recently migrated from the southern part of the United States where health practices differed from those in Connecticut; for example, home deliveries by midwives is a common practice. It was thought important to reach these newcomers with health information they can use—the first step before one could expect to see improvement in the general health of women of childbearing age and the subsequent reduction in complications associated with pregnancy which contribute to perinatal mortality even in the better hospitals.

2. A study[10] of over 28,000 maternity records of women delivered in the hospitals of Hartford County was made: (1) to evaluate the level of maternity and newborn care in a community; (2) to improve the quality of patient care on obstetrical and newborn services; (3) to develop and demonstrate methods of medical self-evaluation; (4) to test and clarify definitions in use in obstetric and pediatric statistics. The study material included patients and their products of conception delivered and discharged between July 1, 1957 and June 30, 1959.

The study was sponsored and financed by: The American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, the Children's Bureau, the Connecticut State Health Department, the Josiah Macy Jr. Foundation and the Division of Hospital and Medical Facilities, United States Public Health Service.

A Community Study

Staphylococcal infections have been of concern to hosptial maternity and newborn services. Significant advances have been made to prevent colonization of babies in the hospital.[11] There were, however, many other questions that had to be answered. For example, did prevention of colonization with hospital strains of staphylococci decrease the number of family infections that were associated with a carrier infant? The Department of Public Health and Epidemiology of the Yale University School of Medicine with financial support, in part, from the state department of health made such a study.[12] The findings indicate that in families with babies who left the hospital uncolonized by staphylococci, the carrier rate was lower and fewer cases of clinical staphylococcal infections occurred than in families whose babies left the hospital colonized.

Admission To Maternity Units

According to Regulation 202 of the Public Health Code of Connecticut, maternity patients must be kept separate from other hospital patients. However, some maternity patients may at times inadvertently be prevented from receiving care on the maternity service. This may be due to a variety of reasons, such as misunderstanding of the Public Health Code or because of local administrative policy. Following are two examples that will illustrate the kinds of cases that ought to be admitted to the maternity service:

1. A patient who is diagnosed as having a threatened abortion, who is expected to respond to treatment and to carry on successfully with her pregnancy, needs skilled maternity nursing care. The same is true for patients with other complications of pregnancy, such as pyelitis, where a good result is anticipated.
2. A patient who is less than 20 weeks pregnant, who goes into premature labor and delivers a living conceptus, needs the same kind of maternity care during labor and delivery as a patient who is pregnant 20 weeks or more. This is different from a patient who is bleeding and who will need a D&C to control bleeding. Hers is primarily a surgical problem requiring surgical care.

Prevention Of Outbreaks Of Infection Among Newborn

Screening of maternity patients for evidence of infection before admission to the maternity unit is one of the important factors in the prevention of outbreaks of infection among newborns in the hospital. The following illustrates this principle:

A maternity patient with a two-day history of diarrhea was admitted to a hospital in labor. During the postpartum period, her diarrhea continued and she had fever. At this time, stool cultures were taken and she was isolated. When her stool and her baby's blood were found to be positive for a Salmonella organism, the hospital staff realized that this mother should have been isolated at the time of her admission.

ISOLATION POLICIES OF SOME OF THE MATERNITY HOSPITALS

Can infected mothers and babies with certain infections be cared for on the maternity unit without contaminating the unit? The answer is both *yes* and *no*. Necessary safeguards that must be present before a policy of isolation on the maternity unit may be adopted include the following:

An active infectious disease committee with representatives from the essential hospital services.

A well prepared and interested nurse educator who is given responsibility for a continuous on-going program of professional and non-professional staff education related to the spread of disease.

An adequate number of nurses and a sufficient number of single rooms to permit room isolation of mothers and babies, either separately or together.

Continuous surveillance by a designated medical staff member such as a pathologist, an obstetrician, a pediatrician, or a general practitioner to detect early any evidence that there has been a break in technique or that an outbreak of infection exists.

OBSERVATION NURSERIES

The question has been raised as to whether or not it is safe to isolate infants in incubators or bassinets within a regular nursery. In certain diseases where the spread of infection is primarily by contact with contaminated equipment or by hands of nursing personnel, strict aseptic individual technique should be adequate to prevent spread of infection. However, it is difficult to be sure that aseptic technique will always be practiced by all persons around the clock, and at times it may be difficult to exclude the possibility of spread of the infection by air-borne routes. Therefore, most hospital staffs are of the opinion that the practical method for control of disease outbreaks, particularly staphylococcal skin infections and diarrhea, is by separating (separate rooms) infected and suspect infants from non-infected infants.

MICROBIOLOGY OF THE HOSPITAL ENVIRONMENT

Recently two statewide meetings were held to discuss the microbiology of the hospital environment. These meetings were stimulated by an outbreak of infection in a Connecticut hospital,[13] and by reports of outbreaks in hospitals throughout the country,[14] caused by organisms that are present in the environment but that do not cause infection unless they enter a susceptible individual in large numbers by an abnormal route such as the eyes, the mucous membranes or broken skin.

In 1961 a letter was sent to hospitals recommending that a bacteriological survey of maternity units be made.[15] Various hospitals undertook such a survey and recovered a variety of organisms from a number of places including the antiseptic liquid soap solution used for scrubbing hands and arms before a delivery.

The medical staff representing hospitals that had made surveys were invited to meet together to exchange ideas and experiences. Subsequently, a small committee of pathologists and bacteriologists was appointed which, under the chairmanship of Earle K. Borman, director of the state health department laboratory division, together with staff from the maternal and child health section, sanitary engineering and preventable disease divisions, will attempt to develop guides regarding microbiological procedures for environmental monitoring in the hospital and their interpretation. Suggestions as to which surfaces and pieces of equipment should be monitored and at what intervals are also expected to come from this group. Emphasis will be given to such items as anesthesia equipment and suction and oxygen apparatus.

State Medical Society Committees

A physician, and at times a statistician, from the maternal and child health section staff, meet with the various state medical society committees that are concerned with the health of mothers and babies. Included are the Committee on Maternal Morbidity and Mortality and its Subcommittee on Toxemia, and the Committee on Perinatal Morbidity and Mortality. The work with these committees is essentially an extension of the work with hospitals.

PERINATAL MORBIDITY AND MORTALITY COMMITTEE[16]

On visiting hospitals, we obtain information which is shared with the Committee on Perinatal Morbidity and Mortality, such as outbreaks of infections due to unusual organisms, or the fact that in one or more hospitals an unusually high number of babies have developed jaundice before 36 hours of age. When these matters are brought to the attention of the chairman of the state committee, he includes discussion of them on his agenda for the monthly committee meeting. The names of the hospitals are kept confidential.

Also included on agenda are discussions of selected cases presented by chairman of local hospital perinatal committees. Preventable factors are identified and recommendations are made. Certain of these case reviews point to the need, for example, for more information regarding medication during pregnancy, during labor and delivery. A questionnaire has been prepared to seek out what are some of the local practices, and how extensive are the practices that have come to the attention of the committee during their case reviews. When such information is received and studied, the committee will then be able to make recommendations for use by physicians.

THE MATERNAL MORBIDITY AND MORTALITY COMMITTEE[17]

This committee reviews the record of every woman who dies during pregnancy or within 90 days of the termination of pregnancy. Thorough discussion follows to determine preventable factors, if any. Information from these reviews is tabulated by a member of the committee in cooperation with a statistician from the state department of health. The last five-year report, published in 1958, covered the five-year period 1951-1955.[18a] A report for 1956-1960 is in preparation. Some of the highlights are:[18b]

> The obstetric mortality rate decreased almost 19 per cent over the previous five-year period. Hemorrhage is still the leading cause of obstetric deaths in Connecticut. Infection is the second leading cause. (Consideration is being given by the Committee on Maternal Morbidity and Mortality to the formation of an advisory group on the study of infections. Endotoxic shock due to gram-negative organisms is of special concern to the committee.)
>
> Toxemia has been replaced by vascular embolism and thrombosis as the third leading cause of maternal deaths in Connecticut.

Recommendations for consultation for major and minor obstetrical conditions have been developed by the committee,[19] as well as recommendations for the prevention and treatment of toxemia of pregnancy.[20] Case reports of maternal mortality and toxemia are published periodically in CONNECTICUT MEDICINE.

The Institute For The Special Care Of Newborn And Premature Infants

In the spring of 1963, six hospitals were invited to send physician-nurse teams to the first institute on the special care of newborn and premature infants. The institute was co-sponsored by the Yale University School of Medicine, the Grace-New Haven Community Hospital and the Connecticut

State Department of Health. The institute came about in answer to repeated requests from hospitals who wanted to send physician-nurse teams to an on-going premature institute in New York, but teams had to wait for admission. Also, not all physicians who were interested could spend two weeks in New York City away from their families and active practices.

The institute in Connecticut consists of one-day didactic sessions for the combined nurse-physician teams on four consecutive Wednesdays. The physicians then have two one-day practical sessions while the nurses have a one-week supervised experience in the newborn special care unit of the Grace-New Haven Community Hospital. The institute is planned as a semi-annual occurrence.

During the first institute there was discussion of what may occur during pregnancy, labor and delivery, or perhaps during anesthesia or the first hour of life when skill and judgment could make the difference between life and death. There was discussion of some of the ways that babies born with a handicap such as jaundice, respiratory distress or anoxia could be cared for to minimize or prevent a residual neurological defect. Environmental control, use of drugs, and feedings were among the many things reviewed.

Discussions were concerned not only with hospital procedures, but also with community resources including ways that public health nurses and social workers could work with the hospital's medical, nursing and social work staffs for the well-being of the mother and baby.

One of the goals of the institute was to help the physician-nurse teams develop in-service teaching programs in their own hospitals. Following the institute, visits were made by faculty of the institute to selected hospitals to see what they were doing or planning to do; how the faculty might help them, and how to modify the program of future institutes to better meet the needs of participating hospitals.

Comments And Trends

In 1944, a Connecticut Monthly Health Bulletin reviewed some of the problems of maternity licensing.[21] The concerns that confronted hospitals and the licensing staff at that time seemed to be to a large extent related to facilities. Example: Having a room set aside for the sole purpose of preparing and storing formulas, having a refrigerator for the sole use of formulas, providing additional bed-pan sterilizers and more utility rooms to serve maternity units, providing handwashing facilities, extra incubators for premature infants, and resuscitation equipment for newborn infants.

The interest and needs of hospitals change as new improvements are developed. Facilities are still emphasized, but personnel also. The qualifications of the chiefs of departments and maternity nursing supervisors are considered. It is helpful for the maternal and child health staff to read minutes of committee meetings, such as the committee on perinatal morbidity and mortality, and various interdisciplinary meetings between physicians, nurses and administration to learn how hospital staffs work to evaluate their procedures and policies. Information is sought about on-going educational programs for hospital personnel—professional and non-professional.

In 1944, 74 per cent of births occurred in hospitals. Today, 99.6 per cent occur in hospitals. In 1944, there was no idea of the cause of retrolental fibroplasia. Since then, a survey of practices in Connecticut hospitals was done and recommendations made regarding administration of oxygen and examination of eyes of infants who have received oxygen.[22] All hospitals now have equipment for measuring oxygen concentration and departmental policies regulate the maximum concentration of oxygen that may be given.

Some problems of medical care are of an economic nature: Since Blue Cross Hospital Insurance does not cover the complications of pregnancy, one wonders how many mothers refuse hospitalization where this is indicated. How many do not get optimum care at home because there is insufficient homemaking service available in the community? How many who are hospitalized during pregnancy are admitted with a diagnosis that could be interpreted to be a possible medical or surgical complication so that a medical-surgical bed is utilized rather than having this patient cared for in the maternity unit where she belongs? How many patients are leaving the hospital 36 or 48 hours postpartum to avoid the cost of the hospital care? Do all these economic pressures result in less than optimum care to the mother or in increased morbidity for the baby?

In the past year, there has been considerable state and national interest in combining within a single nursing unit maternity patients and selected "clean" non-maternity patients, preferably gynecologic patients. Appropriate professional committees are studying this problem.

Medical and nursing staffs as well as administrators are looking at the strengths and weaknesses of intensive care units for newborns. In theory, intensive care units avoid duplication of skilled nurses in maternity units and in pediatric units since post-operative newborns can be cared for by the same nursing staff who care for premature newborns. Other infants who need special care, such as those with respiratory distress syndrome, would also be admitted to this special care unit. In practice, it is difficult to distinguish where special care begins and where regular nursery care ends, so that much thought needs to be given to admission policies before intensive care units are opened.

Care of high-risk mothers who are having complications of pregnancy is currently receiving statewide attention. Funds authorized through federal legislation may make it possible to develop new services in this field.

The prevention of mental retardation due to phenylketonuria is now possible. A statewide program of detection of phenylketonuria in the newborn period is planned to start during October 1963, which follows a pilot program that involved the hospitals in Hartford County.

It should be noted that although this paper deals purely with hospital problems, the improvement of care to maternity patients and their babies requires action beyond the walls of the hospital. Comprehensive maternity service means having girls reaching the childbearing period in good health and with a foundation of healthful habits; with knowledge of sound health education practices; optimum prenatal care; optimum care in the hospital during delivery and the puerperium; optimum care to the baby; preparation of the family for receiving the mother and baby, using social services, public health nursing and homemaker services as indicated; postpartum examination and care of mother during inter-pregnancy periods, especially for mothers who have had complications of pregnancy.

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Personal Physician

The personal physician should be as adept in the art of medicine as he is in the science of medicine. The art of medicine—a misunderstood, intangible, and abstruse quality—is difficult of both definition and delineation. Undoubtedly there are many factors that play a role in its being. It is frequently and erroneously equated with a compelling bedside manner—one thing which it is not. The art is necessary because of the incompleteness and inexactitude of medical science and the high human variability in response to disease and treatment. Basically, the art of medicine can be expressed as the erudition and wisdom that makes the greatest and most effective clinical use of the science of medicine; as the practice of medicine above and beyond scientific rote; as the prudent and judicious interpretation and application of scientific knowledge in a particular situation in a given patient; as the facile exercise of cold, hard judgment unhampered by bias or emotion; as the ability to be creative and inventive when faced with problems unresolvable by scientific fact or formula. The art of medicine would seem to be an inherent quality of basic intellect and wisdom. In its best form it is most often seen in those who have the background and articulate comprehension of the interdependence and triangular unity of basic science, research, and clinical medicine—in those who are adequately grounded in the behavioral sciences and the humanities—with full understanding of the cultural and humanistic interrelationships of medicine and society.—Zale Yanof, M.D.

Special Facilities For The Management Of The Child With Cancer

David H. Clement, M.D. and Frederick J. Flynn, M.D.

■ In many instances the physician's knowledge of community facilities and his proper referral can be the most important step in the management of a major medical crisis, such as cancer in children.

In the State of Connecticut there are two facilities that devote time exclusively to children's malignant diseases. These are situated at the Grace-New Haven Community Hospital and the Newington Hospital for Crippled Children. Each has a tumor registry approved by the American College of Surgeons and is assisted by the American Cancer Society through its Connecticut service program.

Cancer in children between the ages of 3 and 14 years has assumed the number one position in mortality from disease and is second only to death from accidents. The fact that this is a significant pediatric problem behooves us to have knowledge of facilities and to make the best use of them.

Because of the anxieties and special needs associated with cancer in a child, referral is often sought. In most instances the physician can be more helpful if he has a knowledge of nearby services such as mentioned above.

At the present time many children with cancer are treated in well-known centers outside of Connecticut. Out-of-state treatment has many disadvantages to the patient, family and physician.

A survey of families involved with children treated in distant centers disclosed the following problems.

1. Parental absenteeism from home and work.
2. Insecurity of being separated by distance from the medical center.
3. Cost of transportation and living away from home.
4. Emotional energy expended in repeated trips and long periods away from home.
5. The lack of a local physician familiar with the child's current status.
6. Hardship for patient and family if the disease progresses unfavorably and the responsible clinic is distant.

Conversely, children are more secure and happy when frequent visits are possible from local relatives and friends. Family expenditures in time, money, emotion and energy are reduced and home care can be managed more easily when the child is treated near where he lives. When the patient resides near the treatment center it is generally possible for him to be at home more. Short trips for outpatient visits, including marrow aspirations and transfusions, are better tolerated by even the sick child.

Furthermore, it should be emphasized that in most large medical centers children with malignancies are treated in a fairly similar manner. We have been impressed by this fact in patients who have been treated elsewhere before coming under our care. Communication today is excellent between investigators. Advances in the techniques of diagnosis and treatment are promptly disseminated. A child's chances for survival or days of morbidity are not apt to be affected significantly by seeking treatment for these conditions outside of Connecticut.

The Children's Tumor Clinic
New Haven

The Children's Tumor Clinic at the Grace-New Haven Community Hospital meets every Wednesday afternoon at 1:30 P.M. in the Pediatric Department on the third floor of the hospital, 789 Howard Avenue, New Haven. Here the child has ready access to the personnel and resources of the Yale-New Haven Medical Center. The children's wards and pediatric laboratories of the hospital are adjacent to this area.

In the clinic are pediatricians interested and experienced in the various types of malignancy seen in children. Consultation with surgeons and radiotherapists skilled in the treatment of childhood tumors is readily available.

Of special importance is the proximity of the Hunter Radiation Center with its staff of competent radiotherapists. Supervoltage therapy is ad-

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ministered through the 2,000,000 volt van de Graaf electrostatic generator or the 6,000,000 volt linear accelerator, equipment found in few centers. Furthermore, in the Isotope Division diagnostic and therapeutic procedures of great benefit to some children can be performed.

A significant feature of the Medical Center is the extensive and intensive research in cancer chemotherapy that is going on constantly, sponsored by government grants as well as those from the American Cancer Society and other private sources. New compounds of promise continue to be developed. Because of their size, several small children can be treated with the same amount of a new, costly and scarce chemical that would be needed for a single adult.

Through the National Institutes of Health, the Children's General Clinical Research Center has been established on the same floor of the hospital as the Children's Tumor Clinic. Here intensive metabolic studies can be carried out on patients with complex or unusual problems. Furthermore, new antitumor agents can be carefully evaluated under close observation. In this unit these exceptional patients can be studied without cost to the family.

In the Children's Tumor Clinic, patients and parents are assisted by a competent group of social workers. As in the hospital's other clinics, fees are arranged according to the patient's ability to pay.

Inquiries or appointments may be made by writing or telephoning the Grace-New Haven Community Hospital, 789 Howard Avenue, New Haven. Telephone 562-1161, extensions 789 or 760, or make a personal call to Dr. David H. Clement or Dr. Alan C. Mermann.

The Children's Tumor Clinic Newington

The Children's Tumor Clinic at the Newington Hospital for Crippled Children meets weekly on Tuesday at 2:30 P.M. The purpose is for the diagnosis, treatment, and follow-up of all types of tumors. Nonmalignant tumors are also handled.

Pediatricians, hematologists, medical and surgical oncologists meet as a team regularly in the conduct of the clinic. Each case is reviewed by the team at each visit. Bimonthly the team reviews all cases with the radiation therapists and pathologists who are trained in the treatment of childhood tumors.

Every effort is made to treat these patients on an outpatient basis; for those needing it, complete inpatient care is available at Newington Hospital for Crippled Children with a medical staff encompassing all specialties. Admitted patients continue under the supervision of the Tumor Team. Arrangement with the Hartford Hospital brings to patients the latest methods in X-ray therapy including cobalt radiation equipment.

The consulting staff and certain other team members are actively engaged in research, not only at Newington but at other centers, assuring the Children's Tumor Clinic of access to the most recent advances in cancer care.

Patient fees are arranged according to financial ability. An active Social Service Department helps the physicians meet family needs and problems.

Inquiries and appointments may be made by calling the Newington Hospital for Crippled Children, 666-2461, Tumor Clinic extension 285, or by a personal call to Dr. Frederick J. Flynn, extension 235.

To be worthy of the name an experimenter must be at once theorist and practitioner. While he must completely master the art of establishing experimental facts, which are the materials of science, he must also clearly understand the scientific principles which guide his reasoning through the varied experimental study of natural phenomena. We cannot separate these two things: head and hand.—Claude Bernard, *Introduction to Experimental Medicine.*

Meningitis In Newborn Due To Proteus Mirabilus Associated With Intracranial Hemorrhage

Report Of A Case

Noah Barysh, M.D., F.A.A.P. and Ernest Izumi, M.D.

■ Meningitis in the newborn infant is a formidable problem. The prognosis is little better today than thirty years ago despite modern chemotherapy. Bacterial meningitis is seen more often in the first month than at any other time in life. Neonatal meningitis comprises 0.5 to 4.0 per cent of unselected autopsy material. The problem therefore deserves intensive study to reduce the high mortality of a potentially curable disease.

One is impressed in reviewing the literature that meningitis in a newborn is very difficult to diagnose and is usually established by exclusion, especially when the infant is seemingly doing well. The disease is 88.5% fatal in prematures and is associated with some degree of maternal disease in utero. Obstetrical complications were found in at least 56% of a study group and occurred in 94% of cases referred from Cincinnati General Hospital where more detailed birth records were available. The most commonly encountered complication was prematurity, the second most common complication was premature rupture of the membranes. Of seventeen (17) infants in whom the disease began before the 6th day of life, fifteen were born with obstetric complications. Fifteen of the twenty-two (22) patients with onset after the 6th day were born without such complications.[1] The role that infection of the umbilical cord plays in meonatal meningitis has been emphasized by several authors (Potter[2] and Schaffer[3]) and it appears that this was the situation in the case to be presented.

Proteus mirabilus, as a cause of meningitis in the newborn, is extremely rare. Twenty-four (24) cases have been reported in the world literature up to 1957. The first case of this type of meningitis to be described in the American literature was reported by Tolmas and Winter[4] in November, 1957. The case history to be discussed, is the second reported fatality due to this organism in the United States.

Case History

A white female, 5 lbs. 7 oz., 18 inches in length, was admitted to the nursery of the New Milford Hospital on August 6, 1961 at 1:30 P.M. The mother, age 34, with a previous delivery of a premature infant in 1957, had no apparent illness during this pregnancy. She did have spontaneous rupture of the membranes immediately prior to delivery. The labor record was non-contributory: the total duration of labor was 2 hours and 8 minutes. The infant was born by breech delivery and reported in good condition with no apparent congenital anomalies. The mother's postpartum course was uneventful.

In view of the possibility that there might be a problem of isoimmunization in the infant, cord blood was taken.

It was determined that the infant was Group O, Rh positive blood type. A blood level of 6.8 mcg.% of indirect serum bilirubin with hematocrit of 48 and with slight agglutination of Coomb's reagent was obtained on the blood cord. A repeat blood study done 20 hours post-natally yielded 2 mcg.% I.S.B. In anticipation that there might be a subsequent rise in bilirubin, the cord was kept long and moist with sterile saline dressings. The infant was maintained on glucose and water for the first 12 hours and a stock formula of evaporated milk and water was introduced in the usual manner. Fluid intake was supplemented by hypodermoclysis with 2½% glucose and water.

The initial 48 hours of life were normal except that nurses' notes made mention of an odor present in the area around the cord. On the third day of life the infant became lethargic and refused to suck. Temperature was normal and on physical examination the youngster was jaundiced, with good tissue turgor, normal heart and lung findings and with no obvious hyperirritability or change in anterior fontanelle. The blood serum bilirubin determination at this time was reported as 15.4 mcg.%. Intensive hypodermoclysis with glucose and water was instituted (30 cc's q/6 hours). A repeat bilirubin 12 hours later was 19.4 mcg.%. For the first time a slight rise in temperature was noted at 100.4°F. Coincident with this the infant became quite irritable and cried and there was an associated increase in the frequency and amount of stools which became loose and greenish.

Examination on 8/11/61 at 4:30 a.m. revealed an apathetic infant, with a pale yellow skin who cried lustily. Moro reflex was present but with slight flapping of hands and spasm of fingers on the hands. The infant tended to lie on her left side. There was an accompanying grunt. The abdomen was not distended. The heart tones were rapid and regular but the heart rate fluctuated. The lungs were clear. The infant

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was tubed with a polyethylene catheter which was fixed in place in the stomach and esophagus. A clysis was also given. At 8:00 a.m. the infant was in extremis, lying limply in crib with absent Moro and poor sucking reflex. A diagnosis of Meningitis was considered. Material for laboratory study taken at that time is listed. A white count, at 4:00 a.m., August 11, 1961, was 5,400 per ccm. with 14% polys, 78 lymphs and 8 monos. Bilirubin on the same day (8/11/61) was 10.2 mgs.%, calcium 11.6 mb.%, chloride 102.5 mEq/L and CO_2 content was 18.3 mEq/L, phosphorus 10.2 mg.%, potassium 5.3 mEq/L, sodium 131 mEq(L, sugar 58 mg.%. Urine specimen: non-obtainable. Blood culture: no growth after 4 weeks. Purulent material which had a foul odor was obtained on ventricular tap. This material was later cultured and found to contain Proteus mirabilus. Despite antibiotics the infant died and the final diagnosis was neonatal sepsis with meningitis.

An autopsy was performed and the findings were chiefly localized to the brain, spinal cord and umbilical cord. Examination of these organs indicated a large area of hemorrhage over the left cerebral cortex with organized blood extending over the temporal and parietal areas. Whereas, on the gross appearance the meninges did not appear remarkable, microscopic sections of this material were indicative of an acute meningotic reaction. The brain and cerebellum also had inflammatory reaction within the brain as well as in the meninges. The organism isolated from the brain was Proteus mirabilus. The umbilical cord on microscopic section revealed a large number of leukocytes. Anatomical diagnosis: omphalitis and intracranial hemorrhage and meningitis. The cause of death: meningitis due to Proteus mirabilis.

Comment

Proteus mirabilis, an aerobic facultatively anaerobic, gram negative, organism, usually found in putrifying materials and in fecal discharges, as a cause of death is extremely rare. It is of interest in this case, that after infant was autopsied, cultures taken from the throats of the nurses, attendants and physicians using the newborn nursery, grew out a positive culture for Proteus mirabilis in one of these individuals.

The fact that the mother was an Rh blood type with a questionable titer level alerted us to the possibility that this child might have had to be considered an erythroblastotic infant. This suspicion was heightened by the increase of the serum bilirubin to the disturbing levels of 19.5 mg.% on 3rd day. At no time in the initial 3½ days of its life did the infant exhibit evidence of any signs suggestive of a sick infant. It sucked well, there was no elevation of temperature and stools were normal. No reference was made to any oozing from the umbilical stump. However, the cord was kept moistened with saline solution in the event that an exchange transfusion was to be done.

One speculates that this youngster, with the neonate's limited immunologic ability, made more susceptible to infection by a brain hemorrhage, succumbed to an infectious organism that is usually of limited pathogenicity.

The lessons to be learned from this case are several: (1) prematurity or immaturity contributes to the morbidity and mortality of infant life: (2) sepsis in the newborn may be expressed in many bizarre clinical patterns: (3) lethargy and lack of appetite may be the only symptoms in the newborn: (4) jaundice in a newborn can be due to sepsis, as well as a hemolytic isoimmunization process and (5) a cord kept moist may be a point of entry for an otherwise innocuous organism in a setting such as this particular infant offered.

Summary

An infant, an immature female with high serum bilirubin, developed a fatal neonatal meningitis, due to Proteus mirabilis and complicated by intracranial hemorrhage, symptoms of which were not discernible until the 4th day of life.

Acknowledgement

I wish to acknowledge the help of Dr. John Brigham who assisted me in the care of the child.

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The Doctor And The Teen-Ager

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General Considerations

■ Teen-agers seeking medical consultation come with concerns which stem from the accelerated physical and psychological growth processes of this transitional phase of life. They are no longer children. At times they feel "all grown up," but they are not adults, either. Physically, adolescence begins with the pubertal changes, and terminates with the establishment of mature body structure and physiological function. Psychologically, adolescence is more difficult to delineate. As a working definition, onset occurs with the psychological reactions which usually accompany the physical and physiological changes of puberty. It terminates with the establishment of relatively consistent patterns of behavior representing the individual's adjustment to the adult role in our society.[1]

Physical adolescence, and to a great extent psychological adolescence takes place usually between the ages of twelve and twenty-one. There are however, early maturers, whose pubertal changes occur as early as eight years of age, and also late maturers who demonstrate little physiological maturation until eighteen. Whenever the biological events occur, there is an orderly and predictable sequence of changes in height, weight, strength, body configuration, mental capacities, physiological drives and general interests. The psychological responses appear less orderly, but are understandable and predictable when the physical and physiological experiences are considered in relation to the demands which our society places upon teen-agers.

The psychological growth process is prolonged increasingly for many of our youth, who, as they seek higher education, experience a long period of dependency. This leads Erik Erikson to describe college as "A sanctioned interim between childhood and adulthood."[2]

The adolescent physical growth processes are described by Stuart[3] and Tanner;[4] the physiological and biochemical changes by Heald, Daugela and Brunschuyler;[5] and the problem of illness in this age group by Gallagher.[6] This paper presents some of the concerns and anxieties which differentiate the adolescent from the child or the adult. The physician who has developed through the years a relationship of mutual confidence can offer invaluable service during these years.

Although awaited eagerly to some degree by each child, these bodily changes of adolescence arrive often so suddenly and with such intensity that youngsters experience a state of overwhelming restlessness. Early in adolescence, boys experience a period of chubbiness with deposition of fat over the abdomen, hips, and thighs with associated budding of the breasts. Rapid increases in height and weight occur in the following year. Facial contours change. The entire body becomes robust and angular as facial and body hair develop. There is an associated enlargement of the external genitalia and a deepening of the voice. Penile erections and noctural emissions begin to occur at about this time.

The process in girls, occurring about two years earlier than in boys, is initiated by a broadening and rounding of the hips and a simultaneous budding of the nipples, areolar, and breast tissue. As the breasts enlarge to the primary stage, where fat is deposited, there is a rapid increase in height and weight, the appearance of pubic hair, and a gradual increase in size of internal and external genitalia. Menarche takes place on the average at approximately thirteen years of age in the United States, with an age range of eleven to fifteen years for the majority of girls. A few, approximately three per cent, experience the onset of menstruation either before the age of eleven or after the age of fifteen. Menarche usually occurs after a period of rapid gain in height.[7, 8]

The adolescent's concern about his or her body is well known. This is a reflection of the extensive bodily changes which cause him to feel alien to his body, and also is due to a generalized increase in physiological sensitivity to external and internal stimuli. The individual *is* very different than he was a few months ago. He *is* longer, and more solid, and stronger. His head *is* farther than it used to be from his feet. He does have greater strength. His voice *is* harder to modulate When he sits at his chair at the table, his arms and legs do not fit as neatly as they did formerly.

Genetic, nutritional, racial and ethnic factors influence the time at which these changes occur. The age at the moment of this physiological event has

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profound meaning for children. The early maturing girl, for example, needs to adjust to her bodily changes long before many of her classmates experience even the slightest sign of maturation. The late maturer, on the other hand, looks longingly at her classmates, whose body configuration and onset of menstruation precipitates them into a new intense world of interest. While the late maturing child strives to act like those who have reached a degree of physiological maturity, she lacks the physiological support and bodily appearance to play this role with any realistic feelings.

Boys too, are sensitive about physical changes, as well as their prowess. The variation in age at which the changes in height, weight and strength take place creates many problems. Most boys wish to be able to keep up with their classmates, if not excel, in physical activities. A late maturer inevitably will not excel, or at least not untl it is too late to compete during the high school years.

The concerns about early and late maturation are as often verbalized by parents as by children. However, the young patient's facial expression in response to a doctor's understanding comment indicates that they do have real concern. No matter when physical maturation occurs, children wonder whether they will grow up satisfactorily and be able to fulfill the social and biologic responsibilities of adulthood. The intensity of the physiological changes and multiple social pressures, cause teenagers to feel an urgency about moving forward rapidly. They struggle to work out ways of arriving at a position which will provide satisfaction in using their basic drives, endowment, skills and knowledge in a role which at the same time will bring them recognition and respect from adult members of society. They seek to achieve what Erik Erikson terms "a sense of ego identity."[9]

Adolescents are prone to interpret physical symptoms as indicating an interruption of the growth process. This uncertainty of their status is reflected in the intense concern about such things as acne, temporary breast enlargement in boys, the normal occurring irregularities of the menstrual cycle in girls, as well as considerable concerns about illness. They become frightened at the weakness so often associated with convalescence from illnesses and surgical experiences. Teen-agers either attempt to deny these symptoms and return to full activity too soon, or they become overtly over concerned and immobilized. The increase in the adolescent's capacity for cognitive thinking as described by Piaget and Inhelder[10] enables him to think ahead and to attempt a plan of organization for his adult life. It also increases his sensitivity to any symptom which might, at least in his own mind, interfere with achieving these important goals.

Conference With Parents

Many physicians arrange annual conferences with parents during adolescence. This allows for free discussion. The physician can delineate his plan for continuing professional care. He may wish to discuss the advantages of offering teen-agers the freedom to see their doctor when they feel so inclined. Most parents particularly when they have known a doctor for many years are delighted to support this arrangement.

The adolescent's struggles inevitably create concerns for adults. Physicians who present some of the basic facts of physiological and psychological growth are very helpful. Restlessness, feelings of elation and depression, fleeting interests, "crushes," concern over one's body, ardent desires to improve the world over night and explosive reactions to parental restrictions characterize teen-ager behavior. Parents strive to blend permissiveness and freedom of action with helpful restrictions and guidance. This is an increasingly difficult task since today's pattern of social activities in the teenage world bear little resemblance to that experienced by adults when they were adolescents. Parents need to know that teen-agers, who rebel at whatever restrictions are imposed, do appreciate knowing parents' stand on a particular issue. Teen-agers want these limitations, even though they also may need to rebel against them.

One of the most difficult adult tasks is learning to respect a young person's need for alternating dependence and independence. At one moment he will confide and talk freely with adults, while the next moment he wants complete privacy of thought and action. Parents sooner or later discover that there are many times when their teen-age children are uncomfortable toward them. The relationship becomes charged with intensities due to increases in physiological drives. They note that it becomes increasingly difficult to talk freely with their children about sexual matters, reporting "He says he knows it all" . . . "He's not interested" . . . "He walks out of the room when I try to discuss it." What the child knows really, is that his thinking about sexual matters is now accompanied by feelings which cause him discomfort as he discusses these areas with his parents. The fantasies which are associated with penile erections, nocturnal emissions and masturbation are usually too intense and frightening for a boy to discuss with either parent.

Parents need to know that this tendency to withdraw is part of the true nature of adolescent growth. They can be most helpful by providing the kind of a relationship desired by the child. It is not easy to know what phase of dependence or independence a child is experiencing at any given moment. Parents at times will make mistakes. This is inevitable and forgiveable. Anna Freud describes this phase of life saying:

> "It is normal for an adolescent to behave for considerable length of time in an inconsistent and unpredictable manner; to fight his impulses and to accept them; to ward them off successfully and to be overrun by them; to love his parents and to hate them; to revolt against them and to be dependent on them; to be deeply ashamed to acknowledge his mother before others, and unexpectedly, to desire heart-to-heart talks with her; to thrive on imitation of and identification with others while searching unceasingly for his own identity; to be more idealistic, artistic, generous, and unselfish than he will ever be again, but also the opposite: self centered, egoistic, calculating. Such fluctuations between extreme opposites would be deemed highly abnormal at any other time of life.[11]

The social relationships with the opposite sex (i.e. dating, attending dances, necking, petting, etc.) concern parents greatly. There is a tendency throughout America to initiate dating and dancing at an increasingly early age. Many parents assume that children in their early teens are ready for single dating and unchaperoned parties. Other parents, may feel uneasy about this permissiveness, but do not wish to be criticized or be called "squares" by their children. Hence they go along reluctantly with the permissive attitude which they believe is characteristic of other parents, even though discussion often reveals that they are all equally uncomfortable about this state of affairs.

Physicians should explain that young teen-agers, and many older ones also, have not lived long enough to be able to cope alone with the intensity of the sexual drives. To place a thirteen or fourteen year old youngster in a position of handling these forces alone is as cruel as to place a teen-ager at the controls of a jet plane. Stimulated by highly charged movies, TV programs, seductive clothing styles, magazine love stories, availability of liquor and absence of parents from home, teen-agers may find themselves in the position where casual controlled physical contact, such as holding hands, dancing, and fleeting kissing is replaced by physical intimacies leading to the arousal of sexual urges which youngsters are unable to handle physically or psychologically in an appropriate manner. As a result young people frequently become involved sexually before they have matured to the level where sexual desires and intimacies can be experienced as part of an adult relationship characterized by mutual respect, loving companionship and the idea of home and family. Parents need guidance as to the appropriate time for encouraging various levels of social activities. All too often parents wishing to help their daughters enjoy popularity will push them prematurely into the social whirl.

The members of a Senior High School Church group were asked recently how their parents might be more helpful to them. Their answers, "They shouldn't push us so fast" . . . "They make us take dancing lessons in the fifth grade" . . . "They urge us to date when we are not ready for the experience . . ." emphasize that a re-evaluation of adult's responsibility is needed desperately. Adults need guidance so as not to be caught up in cultural pressures which force children into social situations for which they are not ready. Children themselves recognize this is unwise.

Conference With Teen-Ager

The conference alone with the adolescent following the parental conference indicates to him that he has reached a point in life where his concerns are regarded with respect in a one-to-one relationship, rather than mediated, as previously, through his parents. To be successful in this role, the doctor needs to approach his young patient with great sensitivity. Every question needs to be considered as seriously as though it were a life and death matter. A smile at the wrong moment, or any suggestions of joking, teasing, or condescension during the visit conveys the impression that the doctor is not accepting his patient's concerns seriously. Under these conditions, neither the patient nor the physician can continue the relationship to an optimal degree.

As the physical examination is performed, one senses a chief concern: "Is my body all right?" The adolescent wonders "What is happening to me? Are you certain that I am developing satisfactorily? What are these strange body sensations that come and go?" These concerns are exemplified during ausculation of the heart and the measurement of the blood pressure when almost invariably teenagers ask "Is it all right?"

Early maturing children wonder why their body development is so much more advanced than that of their friends. The accompanying physiological drives create restlessness which is discomforting. They cannot discuss this with friends who have not yet reached this level of development. Yet youngsters of a comparable physiological state who are older chronologically spurn their companionship because of their psychological and intellectual immaturity. An understanding comment such as "You have developed a little earlier than many of your friends. I know that you must wonder if your body is in good condition. You seem just fine to me" . . . is reassuring.

Late maturers also need special attention for they too, are ill at ease. Their experiences are difficult because social pressures, such as dating patterns, school dances, tendency to "go steady" literally drag children into activities for which they are far from ready. Even the most minimal signs of physical maturation (i.e., budding of the breasts presence of sparse pubic hair) should be pointed out to the child as evidence that the body changes for which he is waiting so impatiently are about to appear.

The adolescents' physiological sensitivity to body discomfort combined with their concern about growing up adequately causes them to worry about symptoms which earlier in life are considered inconsequential. For example, the chest pain which occurs often following exercise stimulates the questions "Is my heart all right? Will I have a heart attack?" Cyclical abdominal pain commonly experienced by girls prior to menarche arouses worries as to "When *will* my period come? What will it be like? Will it be painful?" Similarly, skin blemishes arouse questions like "What's wrong with me? Is something 'bad' coming out?" The weakness during convalescence from illness or surgery frightens adolescents who interpret the normal weakness as indicative that they are no longer developing. These concerns assume immense proportions.

The annual conference provides opportunity to aid the adolescent to understand and to deal with the sudden increase in intensity of the sexual drives. The physician's role must be clarified, of course, in an earlier parent conference. As a child reaches adolescence, both he and his parents discover that it is increasingly difficult to discuss freely the questions and concerns which arise in the area of sexual maturation and relationships.

Adolescents do possess a great deal of knowledge about sexual matters. This has been accumulated over the years from conversations with parents and school friends, from books, magazines, and also out of the individual's own day dreams and fantasies. Most teen-agers are confused in their understanding of sexual relationships. An eleven year old girl who had sat through several school lectures, movies, and Girl Scout discussions on "growing up" recently told me that she knew "something has to get from the gland in the husband's head to the gland in the mother's head, but I don't know how it gets there. Maybe it's through the mouth." Further discussion revealed that the movie had presented the role of the pituitary gland in regulating the maturation of other endocrine organs, and from this, in addition to some of her confused ideas, she had arrived at this belief as to how conception accurred.

Teen-ager's knowledge in this area includes all the misinformation and folklore which is passed on by word of mouth from one generation of youth to the next. In these early years of accelerated growth, the young people are aware of the facts of intercourse and conception, they have not matured sufficiently to be able to think of sexual relationships as part of the total social, intellectual and physical companionship which is experienced by mature men and women. The teen-ager's physiological urges, like many other aspects of his personality, is largely self centered.

What do teen-agers want to know about sex? Basically, they are curious about how the bodily sensations and feelings which are becoming increasingly apparent are related to the sexual experiences of adulthood.[12]

This does not mean necessarily that they are seeking sexual intimacies at the moment. Rather, they are trying to round out their knowledge of human behavior and learn how sexual acts and gratifications fit into the adult relationships of men and women. Sexual intercourse as an act of love involving the highest human capacities to give and take is not even imagined by most children in their early teens. They possess many misconceptions about sex. They are likely to think of force, struggle, and pain as being predominant in the sexual relationship. When they discuss their thoughts, they often conclude their remarks with "I guess it's worth it if you want to have children."

The physician, after discussing his plan with the parent, should present to his adolescent patients a simple, but thorough and accurate description of intercourse, conception, pregnancy and delivery. Young people are acquainted with these biological facts in a muddled confused way. They are grateful for a re-explanation and the opportunity to ask questions in the privacy of their physician's office. They need help in understanding that their ideas about hurting and being hurt as a characteristic of the sexual act represents a common misconception held by young people, and bear little relationship to the reality of adult sexual experience.

Adolescents need to know that it is all right and expected that they will have physiological urges and sexual feelings that are interesting and enjoyable, and yet at times frightening and overwhelming. They need adult assistance in finding ways to achieve suitable social relationships which allow mutual companionship and sociality between boys and girls. At the same time, they need help in learning how to limit physical intimacies so that they are not propelled into stimulating situations which lead to premature sexual experimentation. Today many youngsters are being caught up in social pressures to date, and date intensively, long before they have matured sufficiently to understand the physiological and psychological feelings and sensations which often are evoked by these experiences.

Many youngsters turn to their doctor (or to a minister or any other adult in whom they have confidence) and, referring to physical intimacies which may, or may not include sexual intercourse, ask "Is it wrong? So many of our friends seem to participate in these experiences." Discussion often reveals that the teen-ager is seeking to test out the adult's reaction to these thoughts, rather than seeking specific approval for participating in sexual relations.

Teen-agers deserve to know that without a meaningful relationship of loving and being loved, sexual intercourse is bound to be dissatisfying, and often unpleasant. This experience lacking any of the deeper aspects of mature heterosexual relationships can be frightening. It suggests to the individual that there is something terribly wrong with his or her capacities to respond adequately in this area. The physician can be of enormous value in helping his patient understand that his or her development, the presence of bodily changes, and the awareness of sexual urges, does not mean that he or she is ready or able, to participate adequately in sexual relationships. Despite all the pressures from within the individual, and from society, to become involved deeply with a person of the opposite sex, most teen-agers are relieved and grateful to have their doctor explain the wisdom of postponing sexual relationships and thus support that aspect of their personality which limits their sexual intimacies at this moment in their life. Later, they will be ready, and better able, to make their own decisions as adults. The adolescent is less frightened by his conflicting urges and the social pressures if he has the genuine support and devotion from adults for whom he has respect. Guidance in this sense represents a valuable constructive force and should not be confused with rigid limitations nor ill conceived permissiveness

The adolescent soon becomes aware that his body reacts to these physiological tensions with sensations and behavior which are new and strange and cause discomfort and anxiety Boys for example, may have disturbing erections of the penis in response to stimulating experiences, or day dreams, or even deeply buried thoughts of which they may be quite unaware While nearly every boy has this experience, his associated thoughts may be so frightening, that he cannot confide in anyone. These tensions often lead to dreams and nocturnal emissions which are also frightening.

Often too, these bodily sensations lead to masturbation which is a mechanism of relieving physiological tension. The associated thoughts create new worries. Teen-agers, and many adults too, think of masturbation as causing skin rashes, weakness, damage to the mind, and interference with later sexual adjustment. The physician who, in a matter of fact way, explains that the experiences represent normal ways for the release of tension during the in between stage from childhood to adulthood, can relieve an enormous anxiety which torments most teen-age boys to an extent that is almost beyond endurance.

Summary

The physician who is able to maintain a relationship which allows parents of adolescents and the teen-agers themselves, to turn to him for understanding and guidance offers invaluable professional service. At no other moment in a family's life cycle are the two generations in need of so much simultaneous guidance as they attempt to work out their relationships so as to achieve healthy adaptations to life in our society. Professional support at this time offers a great opportunity to be helpful to both parents and young people.

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Radio Transmission Of Fetal Electrocardiography And Intrauterine Pressure

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■ Electronic technics enhance the armamentarium of the clinician for elucidating significant parameters associated with physiologic processes of childbirth. Apparatus, especially developed in recent years[8,9,11] for continuous monitoring and recording of fetal heart activity during labor and delivery, can provide objective information free from limitations inherent in customary periodic stethoscopic auscultation.[10] The value of fetal electrocardiography as a diagnostic adjunct and research tool is now widely recognized.[5,10] The FECG aids not only in the determination of fetal life but also furnishes an index of abnormal fetal environment. Variations in patterns of heart activity indicative of fetal distress[4,10] may be accurately detected by methods now available for monitoring and recording. Alterations in the normal parameters of fetal heart rate may supply the earliest clue of the presence of umbilical cord compression, placental dysfunction, abnormal myometrial activity, or impaired fetal reserve. Instrumentation ordinarily employed for this purpose, designed largely for research, is somewhat unwieldy, difficult to transport and often requires extensive cabling. To eliminate some of these disadvantages for wide clinical application and certain specialized investigative procedures, a system of telemetering the fetal electrocardiogram which utilizes miniaturized, more mobile and less costly equipment has been devised. With this technic electrical signals of fetal cardiac energy may be readily transmitted without intervening wires from patients randomly situated on the obstetrical floor to a radio receiver conveniently located at a nurses station for observation and recording.

Radio-electrocardiography was introduced by Holter and Gengerelli in 1949[6,7] as a new technic for cardiovascular studies of the adult. In the last decade sporadic reports of its clinical application have appeared in the literature[1,2] particularly for observations of the effect of exercise or other forms of stress on the heart. Only recently has additional equipment for radio-broadcasting of electrocardiographic data from adult subjects been presented.[2,3]

In the Department of Obstetrics and the Medical Electronics Laboratory at Yale School of Medicine, electronic apparatus has been developed and adapted for radio-telemetry and recording of electrical phenomena associated with cardiac activity of the fetus during gestation and delivery. Accumulated evidence suggests that the relationship of patterns of alteration in fetal heart rate to myometrial activity of labor may have special diagnostic significance. Precise information concerning the frequency, duration, and intensity of uterine contractions is considered to be very important for analysis and interpretation of the data. A technic has been therefore devised for concommittant telemetering of changes in intrauterine amniotic fluid pressure for correlation with the fetal electrocardiogram tracing.

Materials And Methods

The apparatus (Figure I) which has been devised and adapted in this laboratory for fetal radio-electrocardiography consists essentially of a small portable transmitter and a sensitive receiver. External abdominal electrodes or electrodes placed directly on the fetus lead to the transmitter input. The transmitter, now completely transistorized, operates on frequency modulation on a 33 M.c. band to avoid interference present in the conventional 88-108 M.c. spectrum used for other purposes. The radio-frequency portion of the transmitter is fully

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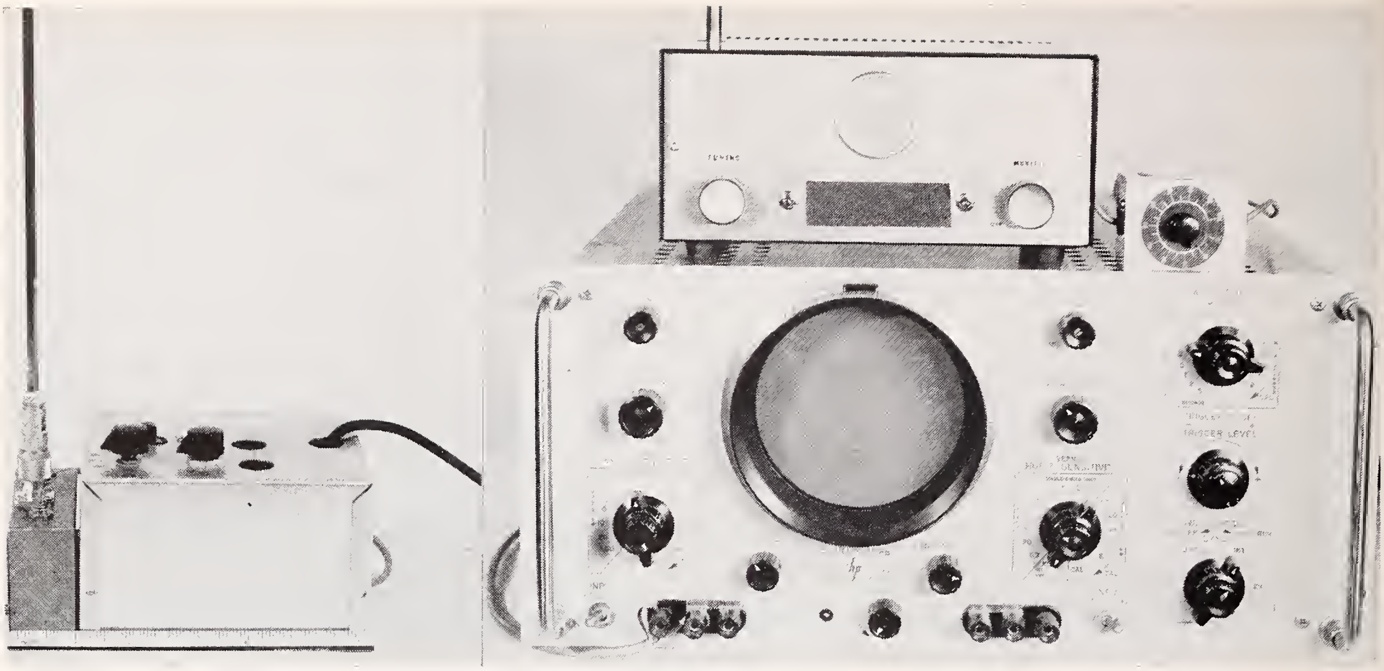

Figure I

Apparatus for telemetering and observing fetal heart activity. Transistorized transmitter (Left). Receiving equipment with osilloscope for continuous monitoring (Right).

transistorized. Pre-amplification was initially accomplished with battery-powered vacuum tube circuitry offering an optimum signal-noise ratio. The preamplifier designed for use with this model has an over-all gain of approximately 2000, a low internal noise level and a high differential rejection ratio. It also has a high input impedance and adjustable high and low frequency filters. The data was transmitted at 10-50 cycles/second. The receiver, using vacuum tubes, operates on a synchronized frequency with a 10 micro-volt sensitivity. It employs an automatic frequency control circuit for stabilization. The receiver which is a conventional FM type has been modified to include a ¼-½ second time-constant in the automatic frequency control circuit. This has been found necessary to maintain the low frequency configuration of the electrocardiogram pattern. Frequency stabilization which is a problem has been perfected with the use of crystal control and frequency modulation. A laboratory prototype model which employs these technics has been tested and will be described later. Presently this appears to be most satisfactory equipment. The output of the receiver is fed into a conventional monitoring oscilloscope and standard recording apparatus consisting of an instantaneous cardiotachometer and oscillograph. Additional filtering which had been incoporated in the pen-writer amplifiers was used for further noise and interference rejection as was required. The original transmitter, having an input power of 40 milliwatts, has a range of 100-200 feet varying with amount of intervening obstruction. Additional power has been added for greater range of transmission as is desired. Successful transmission has been quite consistently achieved and frequently has resulted in improved sensitivity and signal-to-noise ratio. Availability of this apparatus for radio-fetal-electrocardiography permits transitory or simultaneous monitoring of several patients in the delivery area. It may be advantageously employed as a supplement to other less mobile electronic apparatus being used for recording of multiple physiological parameters.

The technic of transmitting and recording fluctuations in intrauterine pressure uses a system of frequency modulation similar to that for telemetry of the electrocardiogram. Changes in pressure are converted to proportional d.c. energy and emitted in terms of frequency deviations. A transducer of the variable inductance type using a moveable ferrite core is employed. The transmitter operates on 60 M.c. band, is crystal controlled, transistorized and operates with a 200 milliwatt input. The receiver is a modified commercial unit designed for frequency modulation. The input signal is appropriately amplified, limited and discriminated for signal reproduction. The system has an overall range of several hundred feet for in line-of-sight operation and has ability to penetrate through several rooms with adjoining walls in the hospital. This crystal control technic has the important advantage of minimizing the detuning problem which may be troublesome in conventional free-running systems.

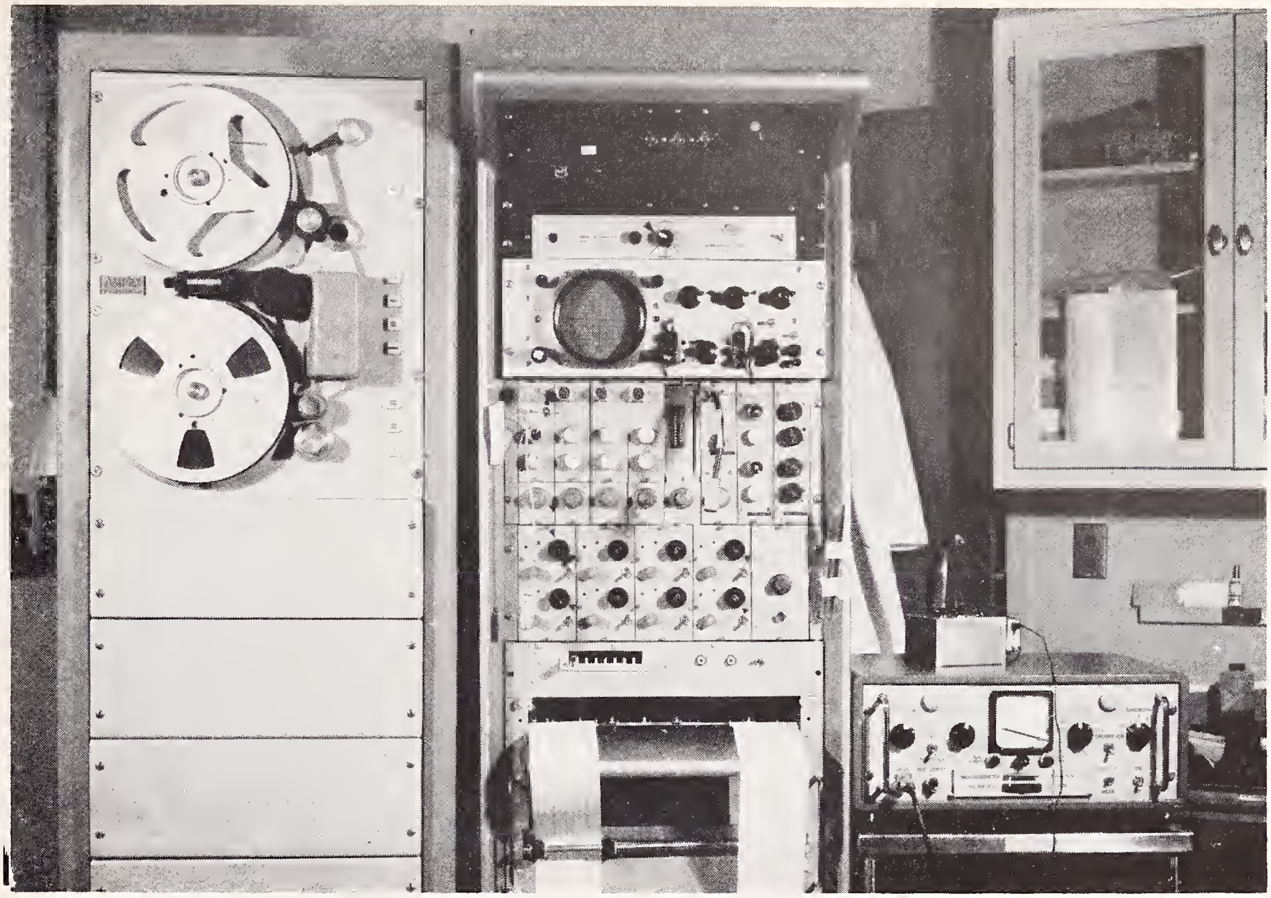

Figure II

Recording apparatus in current use for recording transmitted fetal electrocardiogram and intrauterine amniotic fluid pressure.

Patients And Procedures

Patients included in this study, designed for evaluation of new instrumentation and its application to clinical needs, were selected from patients presenting on the Obstetrical Floor of the Grace-New Haven Community Hospital from June 1961 to January 1963. Over 400 eletrocardiographic tracings were taken for diagnostic or monitoring purposes. The radio-fetal electrocardiograph method was employed as an adjunct procedure to supplement records obtained with standard research apparatus available in the labor and delivery suite equipped for electronic monitoring. The electronic technic was varied and the oscillographic tracings obtained represented testing of methodology and the capability of the apparatus as well as for the usual clinical purpose of determining the fetal heart rate patterns. Suction type electrodes were commonly used although in some instances wire mesh or solder drop electrodes were employed for camparison of stability, noise and comfort. Placement of abdominal electrodes is of importance and may influence markedly the character of the electrocardiogram. A favorable positioning was most commonly found to be in the mid-line; one electrode placed supropubically and the second in the para-umbilical region. When accessible, after rupture of the membranes, an electrode was clipped to the scalp or lower extremity of the fetus. Electrical signals obtained in this manner were picked up by the receiver and fed to the input of a Hon Fetal Heart Monitor, or standard recorders, for oscilloscopic display and ink write-out (Figure II). A few recordings were preserved on an Ampex magnetic tape recorder for subsequent play-back and analysis using a CAT computer. Using standard electronic equipment, fetal electrocardiographic tracings were obtained for comparison with tracings which were recorded under similar conditions on the same patient by means of various telemetering systems. Similarly tracings were obtained to test the efficiency of the system when signals were being transmitted from patients located at varying distances from the recorder. Recently tracings of changes in intrauterine pressure during contractions, have been obtained by radio-telemetry.

Results

With use of the described transmitting technic satisfactory tracings were obtained in the majority of cases included in this study. Poor results appeared to be related to presence of signals of unusually low amplitude, interfering low-frequency inherent skin and muscle "noise," or electrical artefacts from unsatisfactory contact of abdominal electrodes or defective leads. The transmitting apparatus has proven easily transportable to the various labor rooms due to its light weight and compact design. Very little interference was encountered and the electrical signals were quickly picked up on the receiver tuned in on the specific frequencies for electrocardiography and intrauterine pressure. Capability of the apparatus to transmit the fetal electrocardiogram from patients situated at a distance in different areas in the obstetrical ward has been confirmed. Some variation in amplitude of the maternal and fetal complexes is encountered as the distance of transmission or dense walls intervene. This may be overcome by increasing the output of the transmitter, or equilibration effected by adjustment of the gain control. Tracing A (Figure III) was obtained from a multipara in early labor located in a room 150 feet from the receiver and recording equipment. Tracing B was transmitted under similar circumstances from the same patient undergoing strong contractions in late labor. In both Tracings A and B, obtained with the use of abdominal electrodes, the fetal signal was of greater amplitude than the maternal. Although some instability and baseline "noise" occurred during strong uterine contractions, a graph of the fetal heart rate (Tracing C) could be plotted directly from the output of the cardiotachometer.

Fetal electrocardiograms (Figure IV) obtained with scalp electrodes are commonly good. Tracing A was recorded with standard apparatus. Tracing B, transmitted and recorded from the same patient, shows somewhat greater baseline stability with uniformity of amplitude and configuration. The clearly defined signal provided by this procedure simplifies the method of determining the beat-to-beat rate in suitable cases when the amniotic sac has been ruptured. The neonatal electrocardiogram (Tracing C) reveals an irregularity of rhythm with premature ventricular contractions which persisted during the post-partum period in the hospital.

Figure V illustrates types of electrocardiograms recorded by different technics in a twin gestation. Although Tracing A made with standard apparatus suggests multiple pregnancy, a definite diagnosis was difficult. However, the fetal complexes present in the transmitted data (Tracing B) are quite readily distinguishable in this case.

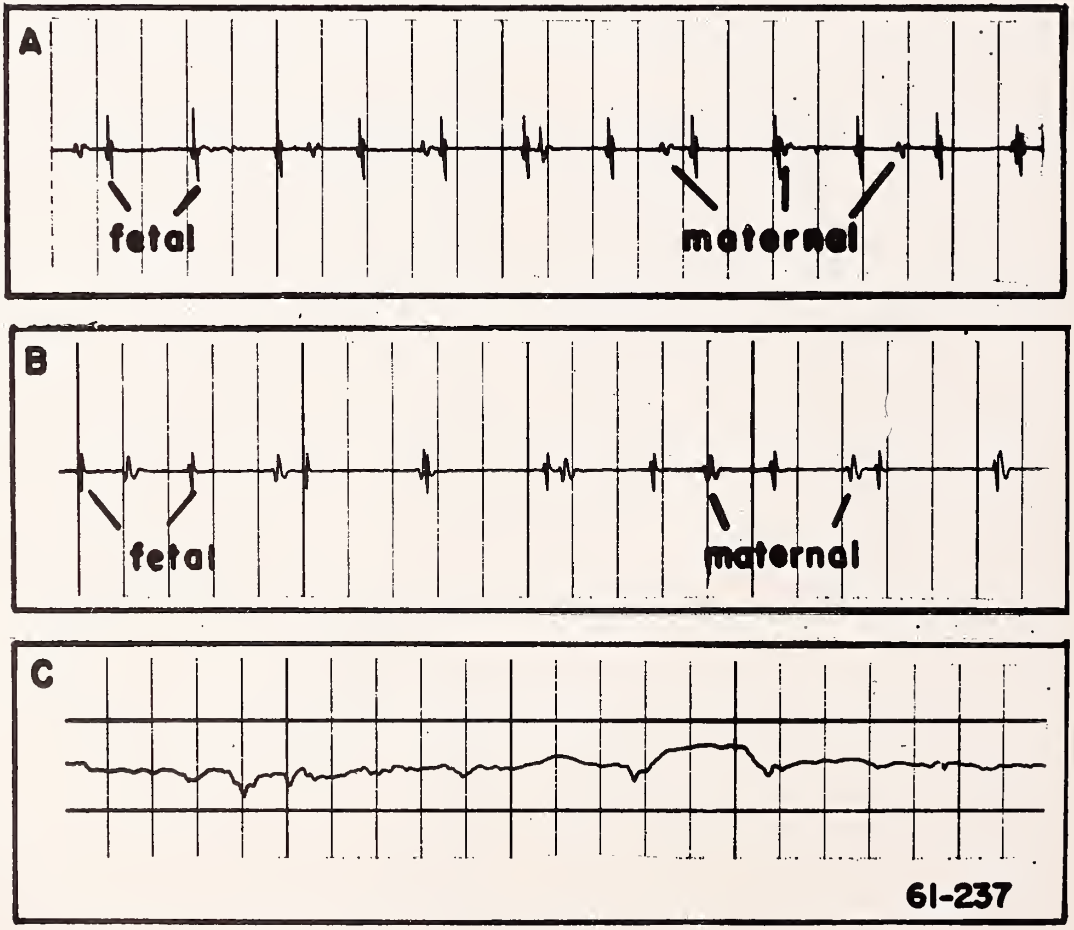

Figure III

The use of radio-telemetry for ambulatory patients is illustrated in Figure VI. The multipara whose tracing during labor is shown was approximately 100 feet from the receiver when Tracing A was made. Some interfering "noise" was encountered in the base line (Tracing B) when the patient moved about.

Figure VII. Tracings of maternal and fetal electrocardiograms were obtained by use of abdominal electrodes and radio-telemetering for simultaneous recording on paper and magnetic tape. The fidelity of the original tracings may be compared with tracings recorded after subsequent transmission several miles via telephone.

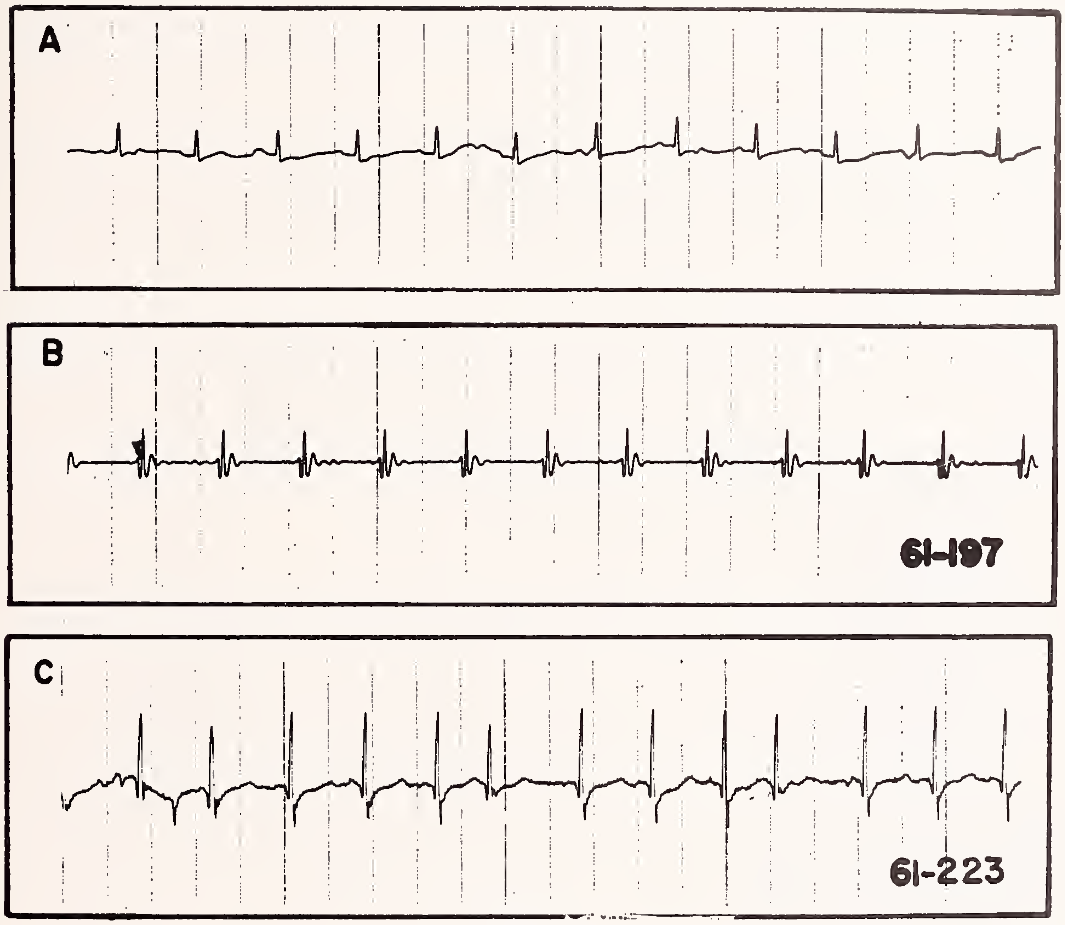

Figure IV

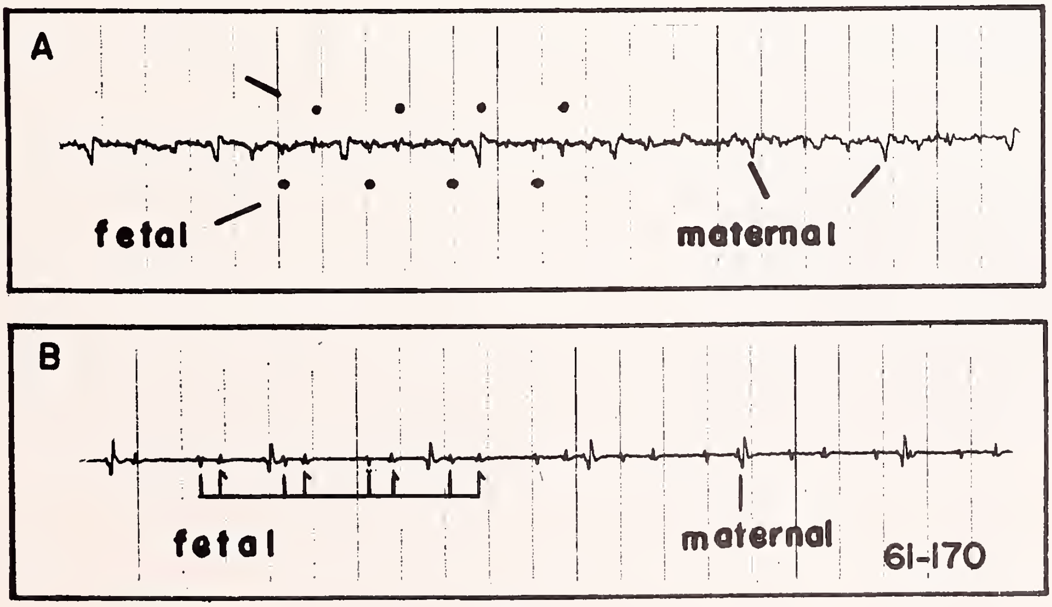

Figure V

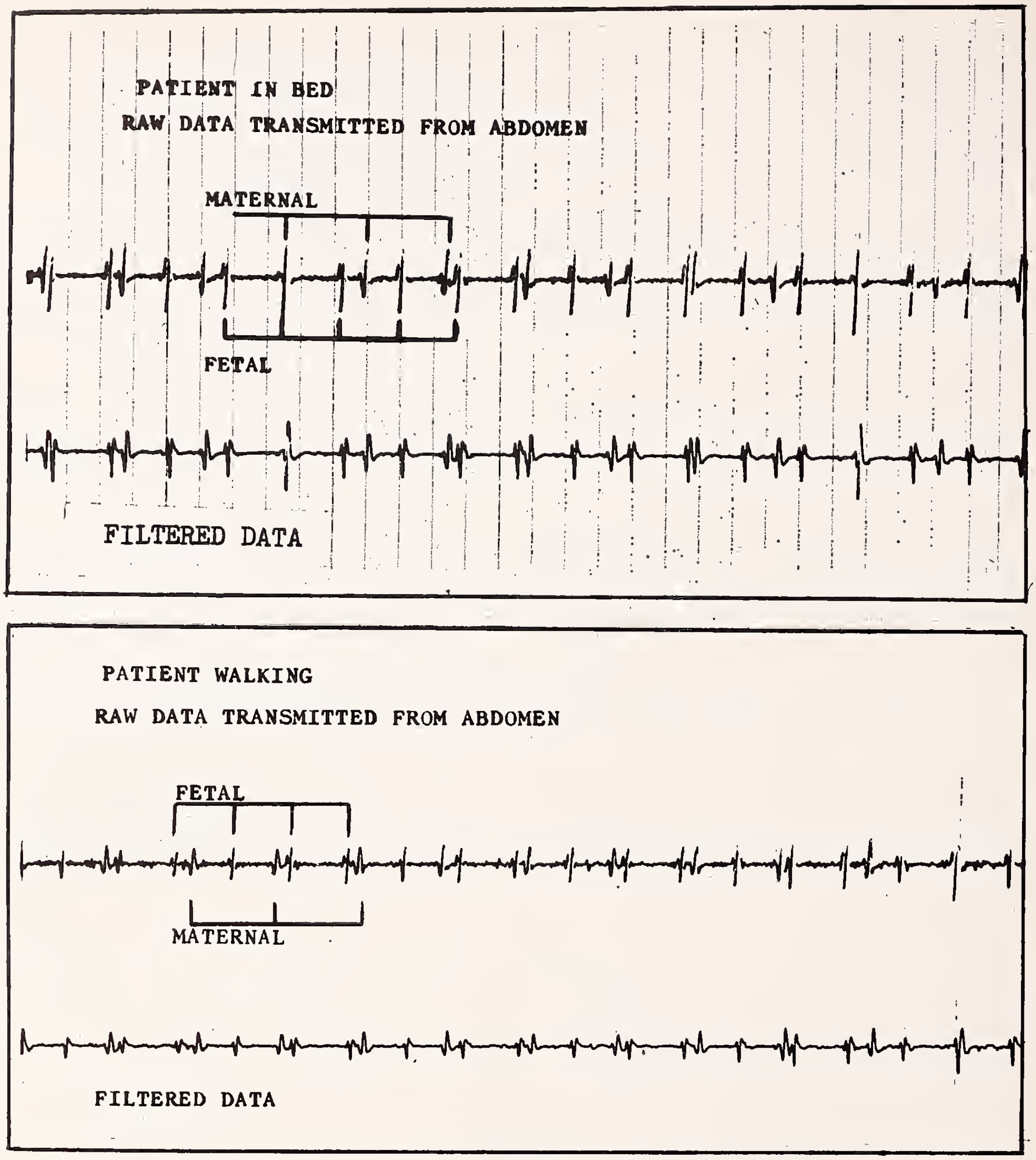

Figure VI

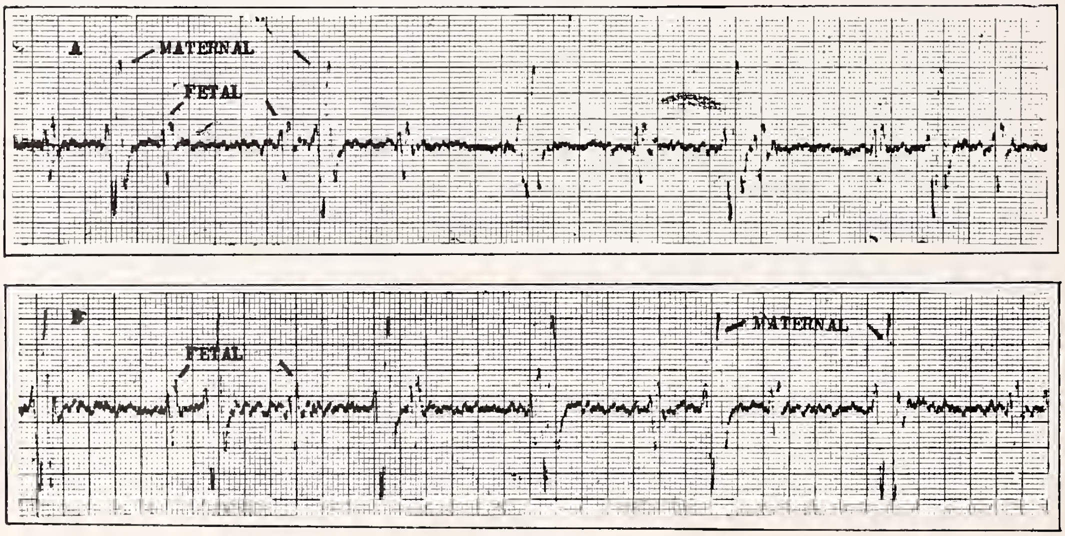

Figure VII
Tracings of fetal electrocardiograms transmitted via radio and telephone. Tracing A after radio telemetering; tracing B recorded after transmission over telephone.

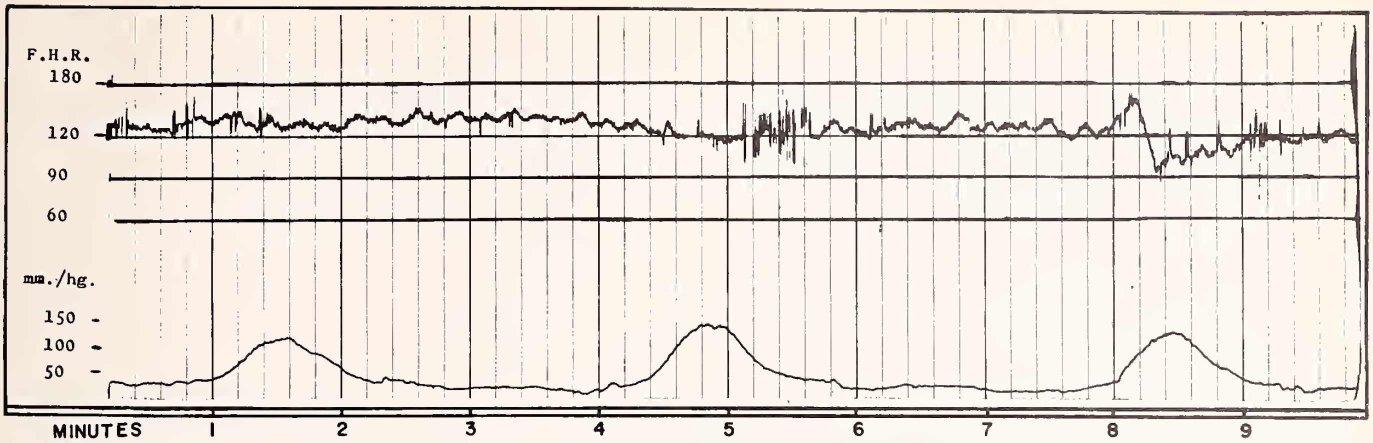

Figure VIII

Tracing A represents the plotted fetal heart rate. Tracing B is a graph of the variations in intrauterine pressure simultaneously telemetered.

Figure VIII illustrates the tracings of fetal heart rate and intrauterine pressures simultaneously transmitted from a patient during active labor. Tracing A is the plotted instantaneous rate while Tracing B indicates the nature of pressure curves encountered with contractions.

Comment

Radio-telemetering is a new technic for the detection, transmitting and recording of fetal heart energy. It has proven useful as a clinical and research tool for monitoring cardiac rate and rhythm offering several obvious advantages. Miniaturized, easily portable apparatus serves the need for quick transfer from one patient to another for brief periodic sampling of heart rate patterns as required. Its light weight permits use for recording the fetal electrocardiogram when the patient is ambulatory. Development of a system of simultaneously telemetering the intrauterine pressure changes associated with contractions is described. Knowledge concerning these parameters may be of value in the early recognition of fetal distress or an unfavorable environment for the fetus. A console type of receiver and recorder for read-out at a central locus can provide a constant source of information of fetal heart activity for nurse or obstetrician in attendance. Data may be tape recorded and coded for preservation and subsequent analysis.

Summary And Conclusions

1. A transistorized transmitter has been developed and adapted for radio-telemetering the fetal electrocardiogram.

2. Light weight, compact, portable equipment suitable for clinical fetal radio-electrocardiography is described.

3. A transistorized transmitter has been developed and adapted for radio-telemetering intrauterine pressure.

4. Electrocardiographic and uterine pressure tracings obtained with developmental telemetering equipment are presented.

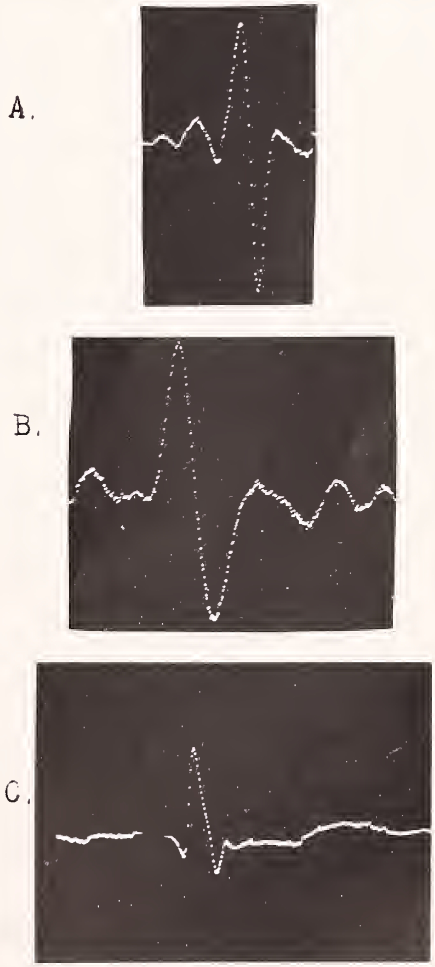

Figure IX

A. Fetal Electrocardiogram after summing with CAT computer (250 m. sec.)

B. Fetal electrocardiogram after summing (125 m. sec.) Note clear definition of waveform.

C. Fetal electrocardiogram after telemetering.

Acknowledgment

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Litter Ships

For a long time we had been flying litter ships, bringing back the wreckage of younger men whose marvelous triumph was breathing. In sharp contrast to the accommodations provided the generals, these ships were always arranged three and four litters high along both sides of the cabin and were always overcrowded. They stank of every elimination which can escape from the human body, but mostly they reeked of quick decay, shock, disinfectant, and blood. Yet none of this seemed to matter, neither the bottles hanging alongside the litters and connected by tubes to the occupants, nor the collapsed areas of blankets where limbs should have been, nor the astonished eyes of a hurt creature peering from a bundle of gauze. Litter ships were an innovation and a majority of the men in them were but a few hours out of combat. Almost before they had time to contemplate their personal disasters they were on the way home. Thus, in spite of wounds, their spirits were unbelievably high and a sort of ecstasy pervaded the whole ship. And the ugliness, which was the reality, was somehow defeated.—Gann, E. K.: *Fate Is the Hunter,* New York: Simon and Schuster, 1961, pp. 309-310.

What About The Incidence of Pediatric Allergy?

Victor L. Szanton, M.D.

■ That the roots of allergy are in childhood has been well established. It is assumed that physicians pay close attention to this hard shell segment of chronic disease because major allergic syndromes such as eczema, seasonal allergic rhinitis, perennial allergic rhinitis and asthma are increasingly apparent. There exists confusion, however, in regard to a valid estimate of the incidence of allergy in childhood. It is the purpose of this report to review the essential literature in order to render guide lines to, and sounder interpretation of, the value of surveys concerning the frequency of allergy in the young and youth of our population. This report is based upon a representative sampling of reported surveys, rather than upon an exhaustive compilation.

At the onset it is proper to suggest that those investigators inclined to biostatistical surveys in allergy be guided by some one previous type of survey. It is essential if some similarities and common ground be trod if one is to be permitted comparisons.

It is also requested that some vested authority in the field of allergy undertake a standardization of approach for clinical surveys as well as interview type surveys. The organized approach is as important to biostatistical studies as it is for all of us to use the same calendar by which to live our daily lives.

Acknowledging traditional attitudes it must be noted that in his book entitled "The Principles of Medical Statistics," Bradford Hill states: "Statistics are curious things in that they afford one of the few examples in which the use or abuse of mathematical methods tend to induce a strong emotional reaction in non-mathematical minds. However great be our aversion, we cannot escape the fact that the vigor of approach to clinical and preventive medicine must ultimately rest upon statistics." It follows then that concern with the problem of allergy in the pediatric segment of our population must, to a great extent, rest upon the assessment of the frequency of allergic disease. Geraldine A. Gleeson of the U. S. National Health Survey Staff in her report on chronic respiratory conditions clarifies the approach as follows:

"Estimates of the amount of allergic illness have been derived from a number of different sources. In general, these source materials may be classified as studies based on medical and clinical records and on examinations, in contrast to surveys conducted by interview. Aside from the general method of study, the basic difference between these two approaches in the measurement of allergic disease prevalence is the underlying concept of morbidity. In medical studies, an attempt is made to detect illness through the use of recognized diagnostic tests and methods, medical history and the presence of clinical signs and symptoms. With the interview technique the objective is to identify conditions which represent a departure from a state of physical or mental well being, of which the affected individual is aware.

"It is quite possible that a condition detectable by diagnostic techniques in a medical examining program will not be reported in an interview because it has had insufficient physical, social or economic impact on the affected individual. On the other hand, a condition reported by a person in an interview because it had interfered with his usual activities may prove to be at a subclinical level at the time of a medical examination. The basic distinction in the concept of illness accounts for much of the difference in prevailing estimates derived from medical studies and those based on interview surveys. The definition of illness in each of these approaches is an inherent characteristic of the technique itself and for this reason the user of such data should not be surprised to find rather marked differences between estimates obtained in surveys of these different types."

Available reports concern areas of varying interest to the authors writing about the incidence of allergy in childhood. None encompasses the entire panorama of incidence. The greatest number of reports stem from medical and clinical studies. These are derived from hospital admissions, clinics, group and private practices. Their geographic spread reflects wide divergences in environmental factors such as local flora or food preferences. They also vary in focus. Some are devoted to asthma only, or to major allergy, or to all allergy, major and minor included. In general the incidence of all categories of allergy, major and minor, in the entire population at large, including all age groups, is traditionally accepted as approximately 50 to 60 per cent. The incidence of major allergy is estimated as occurring in 10 per cent of the entire population including all age groups.

Medical or clinical surveys of the pediatric age group are not numerous but do yield some data.

- I. For all allergies (major and minor):
  - A. Dr. A. J. London, a pediatrician but not an allergist in North Carolina, reports 6.6 per cent of patients in a pediatric practice as having allergy.
  - B. Dr. W. A. Myers, in Hawaii, an allergist, reports 30 per cent in his pediatric practice.
- II. For major allergy only: Dr. W. C. Crook, a pediatric allergist in Tennessee, reports 14 per cent in a group pediatric practice.

Incidence of specific allergic illnesses in allergic children has been cited by clinical surveys for separate allergic syndromes as follows:

- I. Asthma:
  - A. Dr. B. Ratner in New York City reports 63 per cent of all allergic children have asthma.
  - B. Dr. J. Glaser in Rochester, N. Y. reports 53 per cent of all allergic children have asthma.
  - C. Dr. W. A. Myers in Hawaii reports that 51 per cent of all allergic children have asthma.
  - D. Dr. W. C. Crook in Tennessee reports that 33 per cent of all allergic children have asthma.
  - E. Dr. N. Clein in the State of Washington reports 26 per cent of all allergic children have asthma.

Note the large variance from 63 per cent to 26 per cent.

Dr. Susan Dees of North Carolina reports, of all pediatric hospital admissions, 9.3 per cent have asthma. This percentage does not relate to a 100 per cent allergic grouping as do the above, and so cannot be compared with them.

- II. Seasonal Rhinitis:
  - A. Dr. N. Clein reports 38 per cent of all allergic children have seasonal rhinitis.
  - B. Dr. J. Glaser reports 33 per cent of all allergic children have seasonal rhinitis.
  - C. Dr. W. C. Crook reports 15 per cent of all allergic children have seasonal rhinitis.
  - D. Dr. B. Ratner reports 10 per cent of all allergic children have seasonal rhinitis.

Here the figures vary from a 38 per cent high to a 10 per cent low. In contrast—Perennial Allergic Rhinitis presents a larger problem.

- III. Perennial Allergic Rhinitis:
  - A. Dr. N. Clein reports 59 per cent of allergic children have perennial allergic rhinitis.
  - B. Dr. W. A. Myers reports 42 per cent of allergic children have perennial allergic rhinitis.
  - C. Dr. W. C. Crook reports 40 per cent of allergic children have perennial allergic rhinitis.
  - D. Dr. J. Glaser reports 28 per cent of allergic children have perennial allergic rhinitis.

This variance from 59 per cent to 28 per cent shows a prevalence of roughly 2:1 perennial allergic rhinitis as related to seasonal rhinitis.

- IV. Infantile Eczema:

  So far as atopic or infantile eczema is concerned:
  - A. Dr. B. Ratner reports 44 per cent of allergic children have eczema.
  - B. Dr. W. A. Myers reports 39 per cent of all allergic children have eczema.
  - C. Dr. J. Glaser reports 38 per cent have eczema.
  - D. Dr. W. C. Crook reports 34 per cent have eczema.
  - E. Dr. N. Clein reports 33 per cent have eczema.

In general, eczema is present in over one-third of all allergic children. This is an interesting statistic. It shows greater homogeneity of findings than any other of the syndromes reported—the significance of which observation is "up for grabs" and entertaining speculation.

In contrast, we turn to the interview type of survey. These review a broad and relatively unselected sampling of the population. One statistic on the incidence of allergy is culled from the general incidence of illness in school children. Another takes origin from the incidence of all allergy of a school age population. A third refers to the incidence of major allergy only, in children from birth to 15 years of age. A fourth is devoted solely to the incidence of asthma and hay fever. Each has a different approach. One finds the following results:

1. Fitness of Connecticut Youth Survey of 1959 reports 46 per cent of all illness in school children as allergy.
2. The New Jersey Tuberculosis Society reports an incidence of 29 per cent of allergy, major and minor, in school children.
3. Appell, Rapaport and Szanton report an incidence of 23.7 per cent of major allergy in the pediatric age group in a New York-Connecticut sampling.
4. The Department of Health, Education and Welfare of our National government in its Health Statistic Survey reports an incidence of asthma and hay fever as 12 per cent in the pediatric age group.

Here it is noted that in the pediatric grouping a variance exists from 46 per cent to 12 per cent.

A plausible explanation has been offered in regard to the greater percentage of allergy found by interview survey in contrast to clinical studies. One interview survey has pointed out that of those vouching to have major allergy, only one-third had submitted themselves for, or had been exposed to treatment of any sort, no matter how meagre, and that the diagnosis of a major allergy had been made by a physician secondary to an illness or condition other than allergy. In other words, two-thirds of the children within the sampling reported by this survey, known to have, or to have had a major allergy, were never included in a treatment grouping!

It is not remarkable that there are great variations in the statistics. This is to be expected since all the reports have differed either as to method or locale or source of material. The results evoke the ancient adage, "so many men, so many minds."

In evaluating data presented in any survey it is significant that statistics derived are functions of the methods employed and areas represented. Consideration for geographic locale, type of population sampling, centers for diagnosis and means of collecting data is mandatory. A careful scrutiny will permit proper comparison of the findings presented with those previously encountered by the physician reader.

Each physician who is reading a report of any disease must arrive at a conclusion about the relevance of that report to his own private practice. Comparison of conditions of practice, geographical and environment (climate and weather) age grouping, etc. The criteria of sampling upon which the specific report is based is of prime importance. Only by such comparison can any physician recognize the significance and validity of specific sets of statistics for himself and the patients he treats.

With these cautions in mind, one can view the larger picture of similarities in the observed incidence of pediatric allergy. By recognizing the variances and deviations in approach, it is possible to understand and appreciate the differences reported as well as the total pattern of incidence.

As the Bard puts it:

"As many arrows, loosed several ways
Fly to one mark . . . as many several ways
meet in one town; so may a thousand actions
once afoot end in one purpose."

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The cause of human disease never has been and never can be found purely within the walls of a laboratory. There must be at least some association direct or indirect with patients.—Sir Thomas Lewis

Abuse Of Children—Whose Responsibility

Marjorie Toland, M.S.

■ There are abused children in Connecticut. How many and the extent and type of abuse, we speak here of children with physical abuse, is not known. Newspaper stories indicate, as do other media, concern about these injured children. Though the stories give little interpretation about the individual case, newspaper articles and editorials on the subject are bringing to the public an increased awareness of the problem, its complexity and the community's need to provide appropriate and coordinated services to protect and assist children and families.

There are important long term objectives to be considered in order to prevent the development of similar situations. One way may be through the early detection and offer of help to parents, who through their behavior show symptoms that indicate they are unable to care adequately for their children; in some instances to parents, who realizing their uncontrolled feelings towards their child, may themselves ask for help to prevent their mistreatment of the child. Increased lay and professional education, a new and imaginative approach, research on various aspects of the problem including a coordinated community wide demonstration project, may point to ways of safeguarding families and children, and prevent potential abuse situations from occurring. It has been stated that parents seem to fall into three groups: "Neglecting parents who are readily responsive to treatment by the hospital team, neglecting parents readily responsive to a combination of hospital and community services, and unresponsive parents whose childern are in acute danger."[1] Could the parents in the first two groups and, indeed all three groups, be helped before they injure their children for the *first* time? This would necessitate a positive approach toward a subject which until recently communities have more often than not dealt with in a fragmented, punitive, and despairing way.

The need for increased study and understanding of the total problem and for an increased and meaningful coordination of services to families has been shown throughout Connecticut. In Hartford papers in the last six months tragic stories about 11 Connecticut families, involving 20 children or more, have been noted. These children were beaten, dropped, hurled, burned, suffocated, left alone, and grossly neglected; there were severe brain injuries, broken bones, blackened eyes, bruises, and malnutrition. Seven of these children died. Ages of these children ranged from seven weeks to 12 years: eleven of the children were under one year of age; eight of the children were under six months of age.

Most of these children lived in cities, 12 of them in Hartford. One five month old baby girl lived in a small town. The large number of urban families mentioned in the Hartford newspapers differs from the predominance of small town addresses from all parts of the state of 15 families not reported in the Hartford newspapers, but about whom the State Health Department became aware during the same period for a variety of reasons. These by way of inquiries from local hospitals, requests for consultation from public health nurses, and children being seen in the crippled children program of the State Health Department. This difference in locale of residence is one of the many factors about which more information is needed in order to understand and meet the problem on a local and state-wide basis.

The frequent reporting of instances of abuse might seem to indicate that there may currently be an increase of abuse, but it is believed that actually this is because we are hearing more about them. In the preface of a collection of papers given at the National Conference on Social Welfare in 1962, Vincent DeFrancis writes: "Physical abuse of children is not a new problem. The first recorded child protective case (New York City, 1874) involved Mary Ellen, a grotesquely abused child. Although more cases are being found and reported we are not convinced that this necessarily represents a rising incidence. The fact of more cases may be a reflection of greater awareness of a problem, which for long has been ignored and neglected by the community at large."[2]

Though the Connecticut newspaper data about the parents and children, is far from complete, it resembles the data collected in the 1963 nationwide newspaper survey report of the American Humane Society:[3] own parents are largely responsible and involved in the abuse of their children; 73 per cent of parents were not predominantly in

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the younger age group as the mothers' age averaged 26 years, with ⅔rds of the mothers between 20 and 30 years of age; fathers' average age was 30 years with ⅔rds of these fathers between 20 and 35 years of age. This study indicated that one out of every four children died, as a result of their injuries; 54 per cent of the deaths occurring in children under two years of age. Further study of the significance of these facts and others in this material will be illuminated by the followup study which the American Humane Society is undertaking with agencies and others in the communities from which they received newspaper stories. A study will be made of "community approaches toward the protection of the abused child, assessment of community action on behalf of abused children, and evaluation of community attitudes toward the importance of social planning for the child as against retributive action toward the parents."[3]

Meeting the Problem

The observation has been made by Elizabeth Elmer that the methods of dealing with the abused child are "random and inadequate."[4] A clearer definition of what we mean by the abused child certainly needs further consideration and exploration. However, it would appear that the factors influencing these random and inadequate methods are the result of the feelings around the problem which create professional blind spots that make it difficult to approach the problem in a planned way. Society, including physicians, social workers, and others feel a repugnance for the fact that child abuse can exist. The more these feelings of professional people as well as people in general can be recognized and dealt with a greater comfortableness in relating to this problem may permit acknowledgment of a broader definition of abuse. This might include highly charged emotional situations which may not be accompanied by actual physical abuse. We already know that in the case of every child who is physically abused there is a large component of emotional abuse which affects these children throughout their lives.

Radiologists have been in the vanguard of those who created an awareness of the insidiousness of certain types of abuse, as they called attention to the existence of prior injuries to the "battered" child evident through the x-ray examination of children brought to hospitals with a new injury. Dr. John Caffey in lecturing in London before the British Institute of Radiology in 1956 said in his introductory remarks: "My subject was selected over others for several reasons. I believe it to be the least well known and most abused important subject in the entire field of pediatrics and radiology. It is one which I have studied for more than 20 years, one for which I have been able to assemble substantial and, I hope, convincing material."[5] In his closing paragraph he states: "The diagnosis of traumatic injury to infants and children is of more than academic interest, especially when the injuries are repeated and when the traumatic origin is denied by parents or other caretakers. Correct early diagnosis of injury by the radiologist may be lifesaving to some of these otherwise helpless youngsters or it may prevent permanent crippling injuries to others. Early diagnosis may also prevent or stop unwarranted expensive medical investigations which ultimately prove embarrassing to the attending physician, when the true story of simple trauma becomes known."[5]

Hospital Responsibility

Children who are brought into hospitals with questionable injuries are being more carefully diagnosed and evaluated in a comprehensive way but many things add to the complexity of these procedures. For example, if families live in an area where they can secure medical care from a number of different sources (and the parent takes the child some place for medical care) he may be seen successively in several places, thus, possibly concealing the fact that there have been previous injuries. Too frequently these children are the ones who may eventually become severely crippled or killed and neither the child nor the family are saved from this tragedy. The process of learning how to be helpful in these situations indicates that sharing of information and coodination of services is important. If there is some question of the circumstances of the injury, a plan of care involving the family and community is necessary. Sometimes the cause of the injury can be determined and steps taken by the hospital staff, after evaluating the family situation, to help the family according to their individual needs and, when appropriate, with the assistance of other community agencies. Where they had not previously looked together at the problem of abuse of children or had together discussed their mutual concern with outside agencies, the staff of the Children's Hospital in Los Angeles developed procedures in part as follows:

"When the doctor believes that the medical findings indicate inflicted trauma, and the history does not account for the findings, the social worker usually obtains a supplementary history and attempts to evaluate the parent-child relationship and determine whether the parents express any need, or readiness, for help.

A designated full-time medical staff member coordinates all findings, relates them to the history given by the parents, obtains a consensus of doctors that the injuries appear to have been inflicted, and makes a decision as to whether the child should be brought to the attention of law enforcement officers."[6]

The staff of the Boston Children's Hospital is currently working together in the following way: all cases of abuse or suspected abuse are reported to the office of the assistant to the general director. This makes it possible for him to assess the situation, referring to the social service department or to the assigned staff psychiatrist as indicated. A registry of these cases is kept in the administrative office and in the social service office. Their experience is indicating that a definition of what is meant by trauma cases is needed as they have discovered that children may receive physical abuse under a variety of home conditions. Difficulty in coordinating efforts with community social agencies arises when there is a delay in reporting cases where there is a strong suspicion of trauma, and therefore, a delay in studying the situation and taking appropriate action.[7]

These approaches are significant in that they bring together the various professional staff members with the support of hospital administration; in discussing the planning within the hospital, and in discussing and planning with community agencies, including the police, juvenile court, and the legal profession to jointly improve their understanding and activities in the behalf of the abused child and the parents. These relationships are essential, if one is willing to believe that: "parents who neglect and batter their children are actually speaking their parental incapacities in action language, and are asking to be stopped in behaving as they do."[1]

As has been mentioned, it may not be possible for even the most skilled physician to immediately determine clinically whether a child was actually injured, as the circumstances are often far from clear. One of the baffling aspects of this problem has occurred in situations where the parents' appearance and economic circumstances make it most difficult for staff to believe that the injury to the child could have been caused by the parent. Some studies have shown that this syndrome is not found in any one group in a community. "There has been no identification in the multi cultural population of Los Angeles of any significant incidence of injury inflicting, relating to race, cultural background, or religion, nor is it restricted to families with low incomes."[6] On the other hand, in the effort to protect the child it cannot be assumed that every injury is abuse. By so doing one would develop a "Gestapo" type of service thereby adding unnecessary complications and hurt to families.

In the Community

It is possible that in his day by day practice, a family physician or pediatrician may find himself involved with a family in which he may suspect that a parent is not caring adequately for a child or suspects actual abuse. The question may come to him in his office or on a home visit. Can he or does he seek consultation or help from community agencies? Have social workers and social agencies interpreted their services sufficiently to the doctors in the state? Children and family social casework and mental health agencies which offer services to families who seek out their help are also prepared to give consultation to the physician and to help him in helping the family to consider and ask for their services. There are also protective services designed to reach out to families in an authoritative but helpful way when there is a significant weighting in the balance toward probable injury. Maintenance of confidence is observed in these situations.

These services call for especially well trained, sensitive, and courageous caseworkers. They need skill to evaluate the strengths as well as the weaknesses in the family situation. When called upon, they must, if need be involve the police to protect the child as well as the parents. "We recognize that destructive parental behavior of this type is usually symptomatic of deeper emotional problems. Rarely is child abuse the product of wanton, wilful, or deliberate acts of cruelty."[3] This professional casework involvement immediately creates a relationship between a number of people depending on the individual situation: physician, the social worker, the police, the juvenile court, and others who are concerned, such as, the public health nurse, school personnel, the clergy, the legal profession, the hospital staff, and a variety of other agencies that are needed and stand ready to be helpful in a situation. It is evident that much more can be done in the planning, interpretation of functions, and in the coordination of activities to identify, understand, and help the family which needs community assistance to develop a plan with and for them.

Preventive Services

It may not always be the physician who becomes aware that a child is being mistreated. It may be a relative, a neighbor, the delivery man, a guard at the school crossing. How can such individuals be instrumental in initiating help to families? By bringing their concern to someone in the community who can be objective, who will listen to the problem and who can offer suggestions for positive action? Could this service be part of a comprehensive community information and referral service available to the professional person who needs consultation and guidance; to the lay person who is worried and confused as to what to do or not to do in order to help, and also for a family member burdened by a situation he cannot solve? Can we postulate that some of the tragedies that have happened to children were tragedies because there was lack of information and knowledge of how to use community service, both on the part of agencies and the public? Would not such a professional information and referral service help meet this community need? This service could be made available as part of a service dealing with other community needs. Studies of the preventive and other aspects of this problem might be made to include data on how the persons concerned about a family secure information and services.

Delays in families securing services are evident in cases that have recently been brought to the attention of the State Health Department. The widely publicized case of a Connecticut mother indicted for the tragic death of a number of her children which took place over a period of several years raises such speculations. Did the parents at any time seek community services or were they offered to them? There is some newspaper evidence that recently neighbors and agencies had been concerned about the other children. However, do these situations point to the need to clarify what part an individual community member may play in the prevention of child abuse? Do they focus on how professional people, agencies and individuals can work together in identifying the early symptoms of potential family disturbance and disintegration of which the abuse of the child is just one aspect?

Planning Together

The State Department of Health, through its Community Health Division has had an increased interest in this subject for some months, as have many other agencies and individuals in the state. Among other activities, there have been several statewide meetings to explore this subject: one group meeting represented a variety of interests and services; another, social workers from hospitals and residential homes for children. Most recently there has been a maternal and child health advisory committee meeting of representatives of hospital administration, hospital social services, of the medical profession with representatives from general practice, public health, radiology, pyschiatry, pathology and pediatrics, the legal profession, the juvenile court and law enforcement; public and voluntary family and children's and protective agency representatives, public health nursing, and school personnel. Committees are being formed to study various matters raised at this meeting, such as procedures to be used by hospitals in taking a comprehensive and responsible position in relation to the care of these children, the coordination of all community services including medical care and hospitals, the ways of interpreting the subject to the public as well as to the professional workers in this field.

Reporting of cases on a voluntary basis by hospitals and physicians to the health department merits study and may be helpful in this complex problem which necessitates so much cooperation and purposeful action, locally, and state-wide, by voluntary and public agencies. It is anticipated that the committees mentioned above will consider how such reporting and accompanying health department consultation services might enhance and strengthen communications between the medical profession and community social agencies, particularly in those hospitals and communities where everyone is interested in how they can better work together on this problem. Actually, such reporting would contribute to the information on the incidence of these problems. The maintenance of a central registry could also help to detect those instances in which the child is taken to different physicians or different hospitals for separate episodes, thus concealing prior history of abuse. In addition to the reporting, it would be essential, of course, that the hospital staff or, if the child is not in the hospital, the physician, plan for a referral to a community family agency or children's agency, a protective agency, law enforcement officer, or another community agency. Discussion about the implication of these procedures and their integration with the services of all other agencies concerned with the abused child is essential.

Legislation for the protection of the doctor, and possibly others, who may be liable to suit, and the pros and cons of legislation for the compulsory reporting by physicians of cases has been under discussion throughout the country. On the latter subject, the March 10, 1964 Abuse Memorandum of the Citizen's Committee for Children of New York[8] reads as follows: "Finally, we urge that punitive legislation not be passed. Some local communities already have effective reporting and child protective agency programs. Punitive legislation would disrupt, might even destroy, such programs. Other communities should now be given an opportunity to develop sound channels and procedures of their own for the protection of these children and their families. Measures designed to facilitate such programs warrant community support. The feeling that many families can use early and adequate help should stimulate the development of additional and improved services to families throughout the state. To do otherwise is to drive the problem underground; parents may not seek medical attention for their children for fear of legal consequences. And, as we know, physicians cannot be forced to take action which they consider ill advised and potentially harmful to all concerned.[9]

The Future

Study of the roles that community agencies and services can take in contributing to the early identification of potential cases of physical abuse and the clarification of how preventive help can be given is needed in light of the increased knowledge and understanding of this subject.

Protective casework services sufficient in amount and quality to serve families meaningfully throughout Connecticut are needed to cooperate with juvenile courts, law enforcement officers, child placing agencies, hospitals, physicians, and other community services so that an orderly, non-punitive and constructive service can be given to the child and family where there is abuse or suspected abuse.

With a joint approach to the problem understanding as well as communications will improve. "Unless hospitals, physicians, and others can become more aware of the problems, unless communities are helped to understand its causes, and unless the public is prepared to provide adequate social casework and other services to families and children, the reporting would be ineffective.

It is essential that children and their families and the community as a whole be spared these traumatic experiences. Children injured in this way may become a serious and costly responsibility to communities, as they too become unhappy adolescents and adults. Provision of preventive measures stand out as a most important aspect of this problem and one to which community agencies and individuals need to give their best thinking and services."[10]

As in so many efforts where there is an acknowledgment of a problem, a sharing of responsibility and a high purpose much can be done. In this instance the tragedy of the abused child, if it is faced courageously, can be the means through which a happier future for all children who are troubled, including the abused child, may some day become more assured.

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Accidental Poisoning In The Home: A Pediatric Problem

Alexander J. Tutles, M.D. and Arthur S. Blank, B.S.

The Scope Of The Problem

■ More than 10,000 times each year Connecticut pre-school children eat non-edible substances, drink non-potable liquids or swallow overdoses of medications. Many of these incidents result in telephone calls to pediatricians and general practitioners from apprehensive mothers seeking reassurance or advice.

Figure I indicates the extent to which acute poisoning in the home is a pediatric problem. During 1962, of 999 individuals involved in 970 incidents concerning which the Poison Information Center received inquiries, 76 per cent were under five years of age. Similarly, of 1623 patients treated for potential poisoning at ten hospital poison control centers, 64 per cent were in the same age group.

If the product ingested is familiar to the doctor, he can quickly relieve the inquiring parent's fears or, if necessary, initiate measures to cope with a potentially dangerous situation. However, modern technology and marketing have made available a wide range of chemical products, including drugs, for use in and about the home. Since many chemical specialties are duplicated by a multitude of manufacturers, the total number of brand name products that may be found in Connecticut homes runs into hundreds of thousands.

Types Of Potentially Toxic Substances

Figure II illustrates the distribution among groups of household products responsible for inquiries to the Poison Information Center and for potential poisoning cases treated at the ten hospital poison control centers in the state. In each instance, medications led the list quantitatively. The disparity between the hospital-treated cases (69 per cent) and the P.I.C. inquiries (28 per cent) involving drugs is due in large part to the aspirin, barbiturate and other sedative-tranquilizer cases. Only 30 of the 970 P.I.C. inquiries involved aspirin, but of the 1623 hospital-treated cases, 419 (25 per cent) resulted from the ingestion of this analgesic, with few exceptions, by young children. Similarly, the Poison Information Center handled only five inquiries about barbiturate poisoning, but 153 (9 per cent) of the hospital cases concerned this group of sedative hypnotics. Similarly, the non-barbiturate sedatives, hypnotics and tranquilizers (including over-the-counter sleeping preparations) produced 35 P.I.C. inquiries and 170 (10 per cent) of the hospital cases. It should be noted that adults constitute a substantial majority of the patients involved in the latter two classifications.

Value Of Poison Information Centers To The Physician

The physician does not ordinarily find it necessary to call upon a poison center for data on aspirin or barbiturate intoxications. This is not the situation so far as most other drugs are concerned, especially the newly developed ones. In recent years the pharmaceutical manufacturers have come out with many new products—psychopharmacologic agents, diuretics, hypotensives, muscle relaxants, to name only a few types. Shortly after they are marketed, the poison centers begin to receive inquiries concerning their acute toxicities; indeed, some of them have come to the attention of the Poison Information Center while they were still under clinical investigation. Although the manufacturers have carried out exhaustive toxicity tests on animals, these do not necessarily predict the toxic effects of the medications, either acute or chronic, on the human organism. Consequently, the drug manufacturers themselves may not learn the acute toxic properties of their products until cases of acute poisoning are brought to the attention of poison centers.

This has been illustrated at the Poison Information Center. When the Center receives an inquiry concerning a new drug about which it has little or no data, a call is put through to the medical service division of the manufacturer, requesting such information as may be available on the acute toxicity to either animals or humans. Without exception, the manufacturers have been cooperative. By the same token, they will ask the Center to inform them as to the outcome of these cases, or may ask to be permitted to contact the attending physician directly.

DR. ALEXANDER J. TUTLES is Director, Division of Medical Services, Connecticut State Department of Health.

MR. ARTHUR BLANK is Technical Director, Poison Information Center, Connecticut State Department of Health.

National Clearinghouse For Poison Control Centers

The Poison Control Branch, Accident Prevention Division of the U. S. Public Health Service receives reports of poisoning cases brought to the attention of many poison information centers or treated by many hospital poison control centers throughout the nation. All of the poison centers in Connecticut cooperate in this project. This federal agency, more commonly known as the National Clearinghouse for Poison Control Centers has amassed a tremendous fund of data on the acute toxicity of drugs and other potentially toxic household products. This information is disseminated to poison centers and to manufacturers, thence to physicians.

Fulfilling A Need Of The Physician

The physician, confronted with the case of a child who has swallowed some potentially poisonous product often needs more information than he has at his immediate disposal. Among the questions to which he seeks answers are these:

What ingredients does the product contain?

Which of them are potentially toxic?

To what extent is each of the toxic ingredients present in the product?

What is the toxicity of the product as a whole?

What signs or symptoms will indicate the development of acute poisoning? How soon are they likely to appear?

What first-aid measures, if any, should be suggested for home administration?

What emergency medical treatment is required? Is there a specific antidote to counteract the toxic effects of the substance?

What untoward sequelae are possible? Can they be forestalled? What procedures are indicated if they develop?

The search for information starts with the label on the container of the product in question. If the poisoning victim is to be brought to the physician's office or to a hospital, the caller should be instructed to take the product container also.

The label will, many times, list the ingredients. Pesticide labels, for example, must indicate all

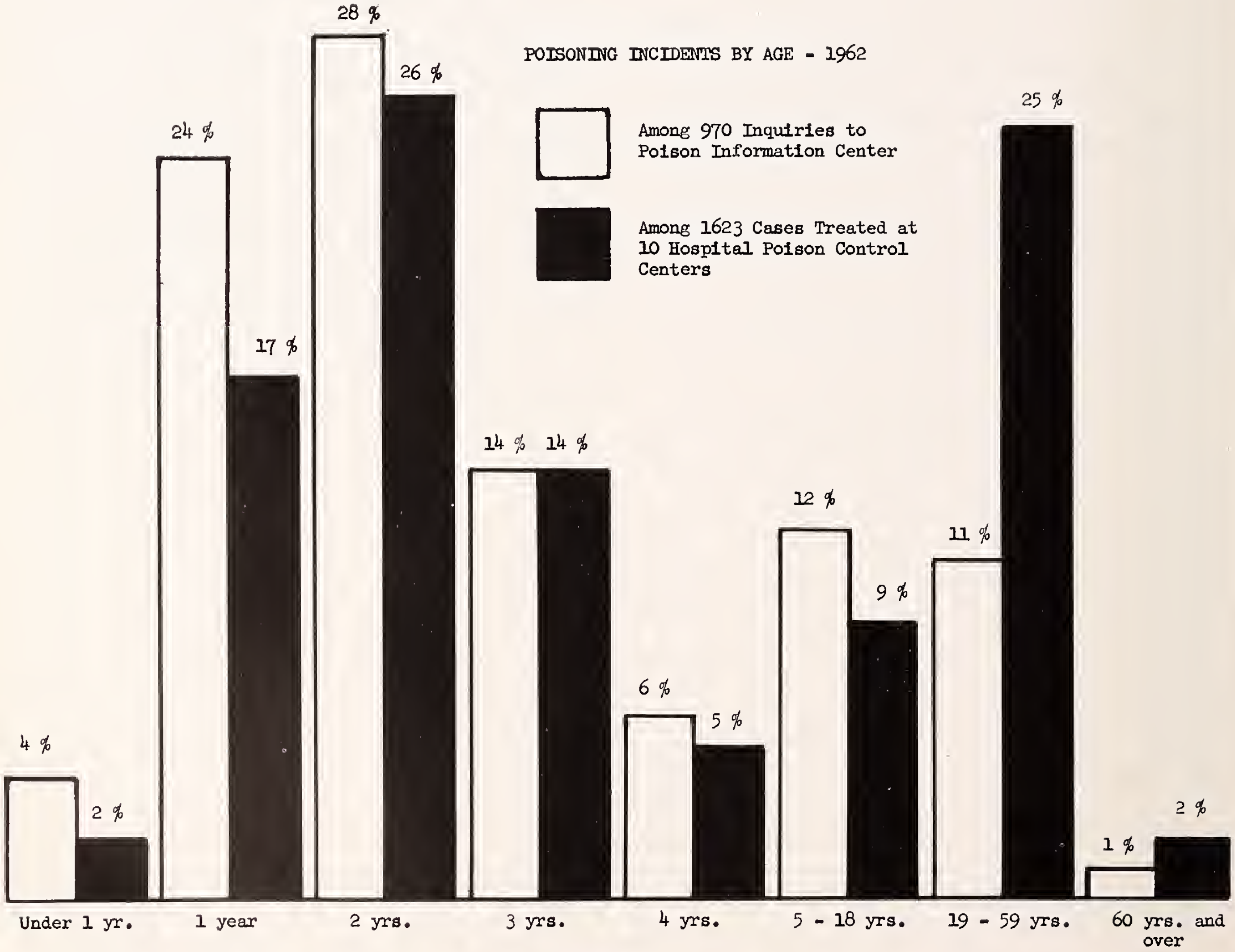

Figure I

active ingredients and their concentrations. Regulations covering other household products may require only the names of the toxic components. By asking the caller for such labeling data, the physician may be able to decide how serious the incident is, whether a simple first-aid measure will suffice or whether medical attention is indicated. It may be pointed out here that cosmetic labels do not require listing of ingredients if the product is non-toxic when used in the manner for which it is intended.

Proper Label Data From Household Products A Necessity

If the physician anticipates calling a hospital poison control center or the Poison Information Center at the State Department of Health about a brand-name product, it is important that he obtain the *exact* brand name and the spelling thereof, as given on the label. How important this is can be illustrated by a product in fairly common use called "Skotch Ice." This consists of a fluid in a can, which is refrigerated prior to being placed in an insulated portable picnic cooler to keep foodstuffs cool. Unless the person who answers the inquiry at the poison center is familiar with this product, he will seek a listing for "Scotch Ice" if he is not given the spelling as it appears on the label. He will then not be able to find the product information in either of two commonly used reference sources, although it actually appears in both as "Skotch Ice." Another such example of "brand-name" spelling is "Klear Floor Wax."

All product labels bear the name and address (city or town) of the manufacturer or distributor. This information may be essential if the desired toxicity data about the product is not given on the label or in the reference sources available to the poison center. The State Health Department Poison Information Center will, when necessary, place a call to a manufacturer anywhere in the United States in order to ascertain the toxicity of a brand name household product. Here too, the *exact* brand name of the product in question is essential, since the manufacturer may formulate a variety of similar products whose brand names differ only slightly.

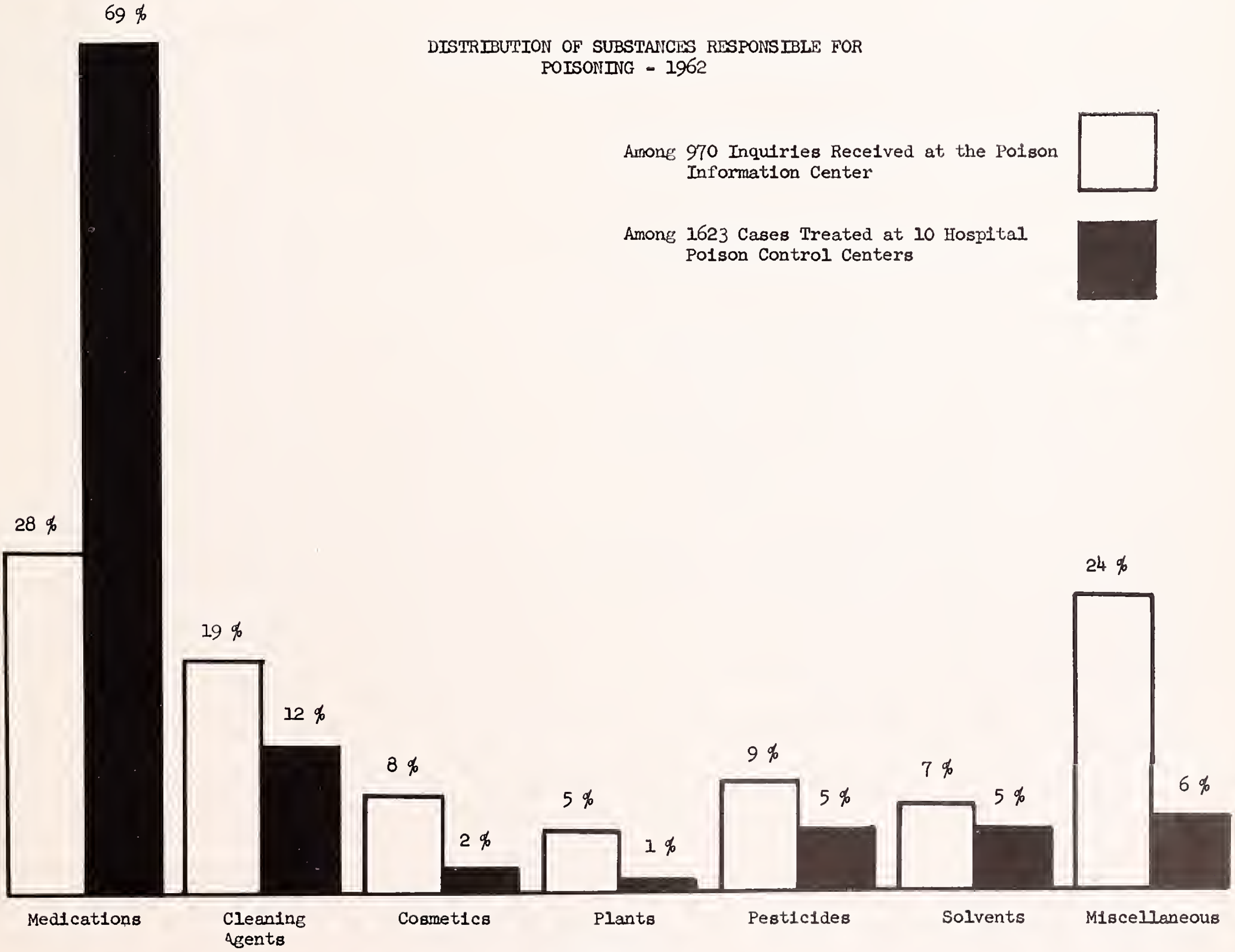

FIGURE II

Not infrequently, the brand name of a product ingested by a child is not available, or the substance may be a chemical or a mixture purchased under a common name. Information about the possible toxicity of such materials may be available from various reference sources at a poison center. The Poison Information Center has prepared a poison index card file that lists toxic properties of brand name products and their constituents, as well as the symptomatology and the recommended treatment of acute poisoning thereby. This file, to which additions are made periodically, has been distributed to the hospital poison control centers in Connecticut. It supplements a similar file prepared and distributed by the National Clearinghouse for Poison Control Centers.

Cooperation Of Local, State And Federal Agencies

Interagency cooperation with other state units, such as the Department of Consumer Protection and the Connecticut Agricultural Experiment Station has, on a number of occasions, provided data on potentially toxic household products which would otherwise not be available. By the same token, the Poison Information Center has alerted pertinent regulatory agencies to the need for more informative labeling or to special toxic hazards requiring investigation.

Insofar as possible, the poison centers in Connecticut provide information service 24 hours a day, seven days a week. The Poison Information Center at the State Department of Health does not have personnel stationed at its office outside of business hours because the number of inquiries received is not sufficient to make this feasible. However, three persons are on call out-of-hours. During 1962, of 970 poisoning inquiries answered by the Poison Information Center, almost half of them were handled outside of office hours. If none of the aforementioned persons is immediately available to answer an inquiry directed to the Poison Information Center, the telephone operator will direct the caller to the nearest hospital poison control center (Table I).

In most cases the physician who calls one of the

Table I

Hospital Poison Control Centers in Connecticut

City	*Name and Address*	*Telephone*	*Director and Ass't. Director*
Bridgeport	Bridgeport Hospital Poison Control Center, 267 Grant Street	334-0131	Russell H. Pope, M.D.
	St. Vincent's Hospital Poison Control Center, 2820 Main Street	366-3601	Leonard F. DelVecchio, M.D. Edward F. Knauff, M.D.
Danbury	Danbury Hospital Poison Control Center, 95 Locust Avenue	744-2300	Robert C. Joy, M.D. Nilo E. Herrera, M.D.
Hartford	St. Francis Hospital Poison Control Center, 114 Woodland Street	249-8281	Stevens J. Martin, M.D. Lloyd N. Hockmuth, M.D.
Middletown	Middlesex Memorial Hospital Poison Control Center, 28 Crescent Street	DIamond 7-2531	Clarence W. Harwood, M.D.
New Britain	New Britain General Hospital Poison Control Center, 92 Grand Street	BAldwin 3-2761	Neil D. Josephson, M.D. Samuel Wolfson, M.D.
New Haven	The Hospital of St. Raphael Poison Control Center, 1450 Chapel Street	777-6581	Norton A. Kazanjian, M.D.
Norwalk	Norwalk Hospital Poison Control Center, 24 Stevens Street	838-3611	Howard K. Ente, M.D.
Stamford	Stamford Hospital Poison Control Center, 190 W. Broad Street	327-1234	Angelo Mastrangelo, Jr., M.D. Clayton B. Weed, Jr., M.D.
Waterbury	St. Mary's Hospital Poison Control Center, 56 Franklin Street	756-8351	Morris Coshak, M.D.

* * * * * * *

CONNECTICUT STATE DEPARTMENT OF HEALTH
Poison Information Center
Hartford 15, Connecticut
Alexander J. Tutles, M.D., Medical Director
Arthur S. Blank, Technical Director
Emergency Telephone: 527-6341 Ext. 456

poison centers will receive answers to his questions about the potential toxicity of the substance ingested. The physician who advises parents on the health of their children obviously must include suggestions for the prevention of accidents, including poisoning. Of course, the young child is prone to engage in oral exploration, and anything within reach that he can put into his mouth is fair game. The careful parent keeps medications and other household chemical products out of the toddler's reach, but many a youngster has exhibited previously unsuspected mental and motor abilities by moving chairs or other objects into a position that has enabled him to climb up and take down containers that had been believed to be beyond his reach.

Human Factors In Accidental Poisoning

Other factors besides exposure to dangerous situations enter into the sequence of events that cause accidental poisonings in children. These include hunger, especially before dinner, when the mother is busy preparing the meal. As previously noted, the child may have achieved an unsuspected level of accomplishment. The mother may be indisposed or ill. The child may be under the care of a friend, relative or paid babysitter unfamiliar with him or with his routine. Parents, especially mothers, must be made aware of the causes of "accidental" poisonings and must be instructed on how to prevent them.

The State Department of Health has available a leaflet intended for use by lay persons entitled "What To Do In Case Of Poisoning." This provides first-aid suggestions to be employed pending the availability of medical assistance. It also offers pointers for preventing accidental poisoning. This leaflet may be procured in quantity by physicians from the department for distribution to parents.

The Zooanthroponoses As Occupational Diseases In The United States

Zoonoses are diseases of vertebrate animals transmissible to man and other animals. Anthropozoonoses are diseases of man transmissible to other animals. Zooanthroponoses are diseases of vertebrate animals chiefly transmissible to man. Every year some two hundred disease entities are added to the total number of approximately three thousand occupational diseases. This increment is more than the aggregate for all other medical specialties combined. It may be doubted that any professional distinction resides in this continually mounting lot of added affections, but the fact reveals the tempo of industrial medicine and the requirement for swift adjustment in meeting increased professional burdens. —McCord, C.P.: *Comparative Medicine in Transition,* University of Michigan School of Public Health, The Lord Baltimore Press, Inc. 1960.

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THE PRESIDENT'S PAGE

The 172nd Annual Meeting of the Connecticut State Medical Society is now history. Overflow audiences at several of the general sessions in the Terrace Room and crowded section meetings attest to the quality of the program. Dr. Allen Margold and his Program Committee are to be commended for a job well done.

The House of Delegates had a long and spirited meeting, the full details of which will be published elsewhere. One of the major items was the consideration of the Council's resolution on the sponsorship of Connecticut Medical Service which read as follows:

Resolved: That the House of Delegates of the Connecticut State Medical Society recognize as a fact that, on January 23, 1964, Connecticut Medical Service, Inc. did disavow the sponsorship of the Connecticut State Medical Society, Inc. by amending the CMS Bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., and confirm that, because of this disavowal, sponsorship of Connecticut Medical Service, Inc. by the Connecticut State Medical Society, Inc, no longer exists.

After a prolonged discussion and presentation of various points of view the House approved this resolution by a very large majority. Since then the question is being asked: What does it mean so far as the Society is concerned? and the corollary question: What does it mean so far as it concerns the individual member who is a Participating Physician? I shall attempt to outline what I believe it all means.

In the first place it means that CMS, by the action quoted in the resolution, did *in fact* disavow the sponsorship of the Society even though it is not spelled out in so many words, and despite the protestation of the President of CMS that this is not so.

It means that there no longer exists any corporate relationship between CSMS, Inc. and CMS, Inc.

It means that the members of the Society will no longer have the opportunity collectively through their elected representatives in the House of Delegates and the Council to present to the Board of CMS their views concerning future contracts, especially as they relate to the schedule of payments and the income levels for service benefits.

It means that any physician who is elected to the Board of Directors of CMS can, in their deliberations, speak only for his own views and cannot presume to represent those of the membership at large.

It means that CMS has established the mechanism for a completely self-perpetuating Board of Directors, and the tenure of office of individual members will depend almost entirely on his own personal wishes, and whether he is dedicated to the principle of extending ever more liberal service benefits to an ever increasing proportion of subscribers.

These are some of the things I believe it means. What then is the situation as it concerns an individual member who is a Participating Physician? Should he remain a Participating Physician or should he resign? This is entirely a question that each physician will have to decide for himself. At the present time each Participating Physician has signed an agreement that binds him to accept, as full payment for his services, the CMS schedule of payments for those qualifying for service benefits on any subscriber contract presently in effect, or that may be issued in the future. And such future contracts, or even major changes in present ones, will be developed by a Board of Directors on which he and his fellow members have no official representation. If he is willing to accept *whatever* the Board of CMS presents to him he will undoubtedly remain a Participating Physician. If he cannot, he has no other recourse but to resign now, or whenever new or amended contracts appear that he cannot accept. The decision is his to make. The old saying about taxation might be paraphrased to read: No service benefits without representation.

Ralph L. Gilman, M.D.

IMPORTANT. PLEASE READ

THE DRAWING OF BLOOD SAMPLES FOR ALCOHOL DETERMINATION UNDER P.A. 616

On May 14, 1964, the Council adopted a resolution concerning Public Act 616 which reads as follows:

BE IT RESOLVED: That the Council of the Connecticut State Medical Society appeal to the members of the Society to accept whatever responsibility is properly asked of them by law enforcement officers and administrators in making chemical tests for alcohol intoxication of motor vehicle operators.

Concerning the "responsibility" to be accepted by the physician who draws a blood sample for alcohol determination at the request of a police officer, a legal opinion was obtained from the Society's attorneys and excerpts from that opinion are published herewith.

PUBLIC ACT 616—IMPLIED CONSENT TO TESTS FOR INTOXICATION

The Act

"In brief, the Act requires a motorist, when arrested for driving under the influence of liquor, either to submit voluntarily to a chemical analysis of his blood or breath or to forfeit his driving privileges. Although the Act is referred to as the "implied consent" statute, the motorist *has the right to refuse to submit to* (*any*) *test,* and the results of the tests can be admitted in evidence against him *only* if consent is given."

"The doctor's cooperation is essential to the successful implementation of the Act, for it specifically provides that if a blood test is taken 'it shall be taken by a person licensed to practice medicine and surgery in this State'."

"The Act also provides that it 'shall not apply to any person whose physical condition is such that, according to competent medical advice, such test would be inadvisable'."

Functions Of The Physician

"It appears that the doctor's function under the Act are limited to (1) deciding whether the physical condition of the defendant is such that the withdrawal of blood would not be inadvisable, and (2) taking a blood sample from the defendant (in conformance with the procedure recommended informally by the Commissioner of Health)."

Insurance Coverage

"We understand that the Connecticut State Medical Society has received . . . an opinion that . . . (Aetna's) standard professional liability policy covers any claims that may be asserted against a doctor as a result of his cooperation with the police in implementing this Act."

Claims Of Assault And Battery

"The Act provides that the results of chemical analyses of blood are admissable in evidence only if, among other things, 'the defendant consented to the taking of the test upon which such analysis is made'."

"It is entirely possible that the person from whom the police want the doctor to take a blood sample will be so intoxicated that he will be incapable of giving a valid consent. The doctor must make his own judgment (of capability) based upon his own observation of the defendant."

". . . regardless of the admissability or inadmissability of the results of the test, it seems to us that a doctor can defend successfully an assault and battery action only by showing that the plaintiff (the arrested person) consented or, at least did not object when he had an opportunity to do so, to the withdrawal of his blood. If the person was unconscious at the time, and thus (totally) incapable of expressing approval or disapproval, this defense can hardly be made."

Minors

"Whether a minor has the legal power to consent to the withdrawal of his blood is not at all clear."

"There is no Connecticut law directly in point on this subject. However, should the question arise in the context of the Act, we think there is a good chance that the court will adopt the more modern and liberal view that the validity of the minor's consent depends upon his capacity to understand the nature and consequences of the medical procedure."

The Nature Of The Consent

". . . advising the accused of his rights is properly the function of the police and not of the doctor . . ."

"However, for his own protection, we suggest that the doctor insist that the person carefully read and sign the following form:

Consent To Taking Of Blood Sample

I hereby consent to the taking from me by ...., M.D. of a blood sample to be delivered by him to the police. I give this consent with a full knowledge and understanding of the following facts:

(a) I have a right to refuse to permit the taking of such a sample.

(b) I have a right to an opportunity to have an additional blood sample taken and a reasonable opportunity to exercise this right.

(c) The results of a chemical analysis of this blood sample may be used as evidence against me in a prosecution for driving while under the influence of alcohol.

I also agree that Dr. .... will incur no liability whatsoever arising out of the taking of this blood sample.

....

Signature

Date: ....

Witness: ....

"If the person is incapable by reason of unconsciousness or extreme intoxication to understand this form, or if he refuses to sign it, the blood sample should not be taken."

Exposure To Liability For Negligence

"The accused's consent to the taking of the blood sample protects the doctor from any liability for assault and battery. However, we think that the accused's 'agreement' that the doctor 'will incur no liability whatsoever' is probably ineffectual to relieve the doctor of liability for injury as a result of his negligence."

"However, his exposure to liability (for negligence) under the Act seems no different from the exposure he experiences each time he treats a patient in his regular practice."

Necessity For The Doctor's Testimony

"It has been suggested that the execution (of the required official forms) will make unnecessary (the doctor's) appearance at any subsequent prosecution for drunken driving." . . . "We cannot agree with this theory."

". . . regardless of the rules of evidence, whether the doctor will be called as a witness for the prosecution will depend in large measure upon the individual prosecutor's concept of how a case should be tried." . . . "The defendant has the right to subpoena the doctor. Whether or not he will do so depends on many different factors, not the least of which is the defendant's attorney's concept of how a case should be tried."

Conclusions

"It is clear that the Act is designed to serve a desirable social purpose. This fact is recognized by the Connecticut State Medical Society's resolution urging all doctors to cooperate in implementing the Act. It is also clear that by cooperating with the police, the doctor can expose himself, or, more accurately, his insurance company, to a possible suit for a technical assault and battery and, should he perform his function negligently, to a suit for malpractice. However, since the damages in any assault and battery suit probably will be limited to less than $1.00 unless special injury can be shown, it seems unlikely that many such suits will be brought. With respect to possible suits for malpractice, the doctor's exposure to liability seems no different from the exposure he ordinarily assumes each time he treats a patient in his regular practice."

"We note, in conclusion, that it might be possible to do away with the doctor's exposure to a suit for assault and battery by a simple amendment to the Act which would provide: 'Such physician shall not be liable for damages, in any civil suit, for withdrawing such blood (sample), except for negligence in the performance of such withdrawal'."

(N.B.: *The Committee on State Legislation has been instructed to introduce this amendment at the 1965 General Assembly.*)

MEDICAL RESERVE OPPORTUNITY

Any Physician of Medical Reserve component has excellent opportunity to build up retirement credit with pay for fifteen days active duty at Niantic, Connecticut, period from 25 July 1964 to 8 August 1964. If interested contact Col. Joseph J. Bruno, Surgeon General State of Connecticut. Write to 1266 Forest Road, New Haven, Connecticut. Tel. 387-5589 or 933-2561.

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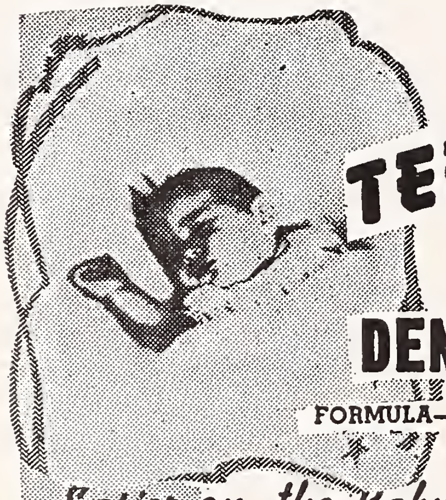

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SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, April 22, 1964

I. Attendance

Present in addition to the Chairman, Dr. Martin, were: Drs. Gilman, Goldberg, Hess, Weise, Sr., Scully, Wilson, O'Connor, Bradley, Grendon, Grant, Davis, Phillips, Shepard, Dean, Ciccarelli, Seigle, Egan, Abbot, Caplan, Spitz. Also present were: Mrs. Lindquist, Mr. Burch, Mr. Nickerson, Dr. Richards. Absent were: Drs. Pitock, Cullen, Gardner, Hughes, Weber, Jr., Gevalt, Hastings, Major. Guest: Dr. J. A. Fabro.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of March 25, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Henry Harper Hart, Southbury (NHCMA)
Kurt Oppenheimer, Norwich (NLCMA)
M. L. Riccitelli, New Haven (NHCMA) beginning 1965

Resignation—Conference Committee With State Bar Association

It was VOTED to accept the resignation of Harold S. Wright, Greenwich, as a member of this Conference Committee, and to approve the removal of his name from the slate of nominees for 1964-65.

Membership—U.S. Chamber Of Commerce

It was VOTED to table action on the question of CSMS joining the National Chamber, pending receipt of further information concerning the possible effects of such action in relationship to the Society's tax-exempt status under its present Internal Revenue Service classification as an educational and scientific corporation.

Appointment Of Chairman—Relative Value Study Committee

Since Benjamin D. Thaw, Hartford, informed the Council that he can no longer devote the necessary time to his duties as Chairman of the Committee on Relative Value Study, it was VOTED to appoint Stewart P. Seigle, Hartford, to replace Dr. Thaw as Chairman of this Committee. It is understood that Dr. Thaw has volunteered to assist the new chairman in becoming oriented to his assignment in order that the project can be completed as expeditiously as possible.

Progress Report—Ad Hoc Committee On Corporate Practice

David A. Grendon, Chairman of the Committee, reported that a ruling on the Blue Cross Rider had been received by legal counsel from the State Attorney General and that the Committee would soon be meeting with Mr. Marcus to discuss the ruling and to determine what further course of action can be developed for recommendation to the Council. The report was received as information.

Progress Report—Ad Hoc Committee On Resolution No. 2

E. Tremain Bradley, Chairman, reported that the Committee is pursuing its assigned task of formulating appropriate prepayment methods for the people of Connecticut. It was VOTED to accept Dr. Bradley's informal report as information and to supply each member of the Council with a copy thereof.

Date Of Next Meeting

The organizational meeting of the Council for 1964-65 will be held on Thursday, May 14, 1964, at the call of the incoming President, Ralph L. Gilman.

III. Old, New And Special Business

Connecticut Medical Service, Inc.

Letters of correspondence between the General Manager, the President of CMS, and the Chairman of the Councid were presented to the Council members in printed form and were reviewed and summarized by the Chairman. In essence, Dr. Martin reported to the Council that it appeared Mr. Coolidge was at last calling a meeting (4/23) of the Board of Directors of CMS to receive the report of its Liaison Committee and to respond to the actions taken by the Council on March 25, 1964. He voiced his opinion that unless something quite unexpected occurred before April 28th, the Council had no choice but to present to the House of Delegates on that date the resolution adopted by the Council on February 15, 1964 (confirming that sponsorship of CMS by the Society no longer exists).

The Chairman then called for reports from county representatives on the actions relating to CMS which had been taken by the several county medical associations at their recent annual meetings. Although not all their actions were identical, it was reported that the memberships of the constituent associations in Fairfield, Litchfield, Middlesex, New Haven and Tolland counties had voted to support the position of the Council as embodied in the February 15th resolution. Conversely, it was reported that the memberships of the New London and Windham County Associations had voted not to support this position of the Council and had expressed a desire that sponsorship of CMS by the Society be continued. Other informal reports were received from several city medical associations, all favoring the action proposed by the Council.

Following extended discussion, a motion was made to re-affirm the resolution of the Council, adopted by voice vote on February 15, 1964, which stated that, by its January 23rd action to change its Bylaws, CMS had disavowed the sponsorship of the Connecticut State Medical Society, and that the Council recommend that the House of Delegates "confirm that sponsorship of CMS by the Society no longer exists" when the House meets on April 28, 1964. A roll-call vote on the motion was taken, and the motion was passed by a vote of 18-4. Those voting *yea* were: Drs. Gilman, Goldberg, Hess, Weise, Sr., Scully, Martin, O'Connor, Bradley, Grendon, Grant, Davis, Dean, Ciccarelli, Seigle, Egan, Abbot, Caplan and Hastings. Those voting *nay* were: Drs. Wilson, Phillips, Shepard and Spitz. The draft of a "Statement of the House of Delegates," which embodied the history, details and significance of the recommended action concerning sponsorship of CMS by the Society, was amended somewhat and then approved in amended form. It was understood that the "Statement," as approved, would have no official status unless and until the recommended action had been taken by the House of Delegates, and that it would be released as public information only after the House had voted to accept the recommendation of the Council concerning the status of sponsorship of CMS by the Society.

Reports—Committee On Hospitals

(a) As requested by the Council, the Committee on Hospitals had prepared a report on "Hospital Costs and Accounting Procedures" and submitted its report at this meeting of the Council with the recommendation that it be approved and transmitted to the House of Delegates on April 28, 1964. It was VOTED to approve the report and to recommend its approval by the House at the Annual Meeting.

(b) The Committee on Hospitals, at the request of a member of the Society, had made a study and prepared a report on the question of third party agencies making payments directly to intern and resident "education funds" for services performed on ward patients under the direction of members of hospital attending staffs. The study revealed that this question must be answered in the negative, according to the State Insurance Commission and others. It was VOTED to accept the report as information, and to direct the General Manager to send a copy to the member who asked for an opinion on the subject.

Recommendations—Committee On Aging

(a) It was VOTED to accept a recommendation of the Committee as follows: "Concerning the MAA (Kerr-Mills) program, the Committee (and the Joint Council to Improve the Health Care of the Aged) feels that the present practice of processing these recipients on the same forms as all other recipients of public assistance is hindering the progress of the MAA program in this State. The Committee recommends that the Council urge upon the State Welfare Department that these (MAA) people be processed separately and on separate forms from recipients of (general) public assistance in order to preserve their identity."

(b) It was also VOTED to accept a recommendation of the Committee as follows: "Concerning the 'Standards for Accreditation of Nursing Homes,' recently published by the National Council for the Accreditation of Nursing Homes, the Committee has studied this document and 'wishes to go on record as approving these standards. . .' " In taking this action, the Council has likewise approved these standards.

(c) It was further VOTED to make this information concerning the accreditation of nursing homes available to the CSMS Committee on Hospitals.

Recommendations—Committee On Public Health

(a) Approved by the Advisory Committee on Nutrition, and by the parent Committee on Public Health, a "Simplified Diet Manual" for use in convalescent hospitals and nursing homes was reviewed. The pamphlet was prepared by the Dietetics Department of the State Department of Health. It was VOTED to approve the pamphlet as submitted, and to authorize use of the endorsement "Approved by the Connecticut State Medical Society" on the pamphlet when it is published by the Health Department.

(b) On recommendation of the Committee on Public Health, it was VOTED to adopt a resolution as follows:

"BE IT RESOLVED: That the Council of CSMS approve a 'Digest of a Proposed State-wide Oral Cytology Project for Connecticut,' such oral cytology project to be conducted by the Connecticut State Dental Association and the Connecticut State Department of Health with the assistance of approximately $30,000 a year for each of three years from the Department of Health, Education and Welfare."

Request For Adjudication—"Overhead Expense Plan"

In response to a request from a Fairfield County member that the Counicl investigate his complaint that the underwriters of this Society-sponsored plan did not honor and pay his claims during a period of disability, it was VOTED to authorize the Committee on Medical Economics and Insurance to conduct a hearing in this matter and to report its findings and recommendations to the Council.

Committee Service Questionnaire

In response to a recommendation of E. Tremain Bradley, FCMA Councilor, it was VOTED to repeat the "Committee Service Questionnaire" mailed out with Connecticut Medicine several years ago and to publicize the mailing in the pages of the Journal several months in advance. Dr. Bradley pointed out that the original returns had been of great help to the Committee on Preliminary Study of Nominations in making committee selections, but that these were now outdated and of no further value.

Chairman Of The Council

A rising vote of thanks was passed and executed in acknowledgment of the superior service of Dr. Martin as Chairman of the Council during the past twelve months.

Memorializing Resolution

It was VOTED to direct the General Manager to prepare a resolution memorializing the death of Joseph A. Fiorito, New Haven; that the resolution be spread upon the minutes of this meeting of the Council; and a copy of same be sent to Dr. Fiorito's family. The resolution follows:

WHEREAS: Dr. Joseph A. Fiorito has performed with distinction as a practitioner of medicine in the City of New Haven, Connecticut, and in many elective and appointive offices concerned with the advancement of the art and science of his chosen profession throughout the State, therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society take cognizance of the death of a distinguished member of the Society, Dr. Joseph A. Fiorito of New Haven, on the 16th day of April, 1964, and convey a message of deep sympathy to his family.

New Members

Fairfield County
- Antonio N. Albanese, Danbury
- Felix J. Callan, Danbury
- Harriet E. Cherry, Stamford
- Kenneth G. Goss, New Canaan
- Donald P. Granger, Stratford
- John I. Larkin, Greenwich
- Kevin F. McCaul, Norwalk
- John J. McKeever, Stamford
- Thomas F. McLoughlin, Danbury

Hartford County
- Albert L. Babcock, Hartford
- Harry H. Browne, Southington
- Michael F. Carr, Hartford
- Stanley W. Edelstein, Hartford
- Victor L. Fortin, Jr., Hartford
- Edward F. Fox, Bristol
- James E. Grassi, Manchester
- Sidney Kligerman, Hartford
- Stanislaw A. Milewski, Manchester
- William E. Palmer, Jr., New Britain
- Nancy R. Powell, Wethersfield
- George E. Reardon, Hartford
- Josephine C. H. Rodriguez, Hartford
- Marvin Saltzman, Plainville
- Alden W. Seleman, Bristol
- Lawrence E. Sereda, Hartford
- Philip A. Shelton, Hartford
- Roy B. Sherman, New Britain
- Mary Anne Tummillo, Windsor
- William B. Waterman, Hartford

Middlesex County
- Anthony L. Dudzic, Middletown
- Burkhard W. Voelkening, Middletown

Windham County
- Blake D. Prescott, Storrs

1964 MEETINGS

June 14-19—The VII Interamerican Congress of Cardiology will be held in Montreal, Canada.

June 21-25—Annual Meeting American Medical Association to be held at Fairmont & Mark Hopkins Hotels and Civil Auditorium, San Francisco, California.

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

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SUMMARY OF PROCEEDINGS HOUSE OF DELEGATES — ANNUAL MEETING

Hartford, Connecticut — April 28, 1964

Reports, Addresses And Remarks

Presentations were made to the House as follows:

Reports

The Secretary: Orvan W. Hess, New Haven

The Treasurer: Isadore S. Goldberg, Torrington

The Chairman of the Council: Stevens J. Martin, Hartford

The General Manager: William R. Richards, New Haven

Addresses

The retiring President: Morris P. Pitock, Bridgeport

The incoming President: Ralph L. Gilman, Storrs

President, Woman's Auxiliary to CSMS: Mrs. Fritz M. Meyer, Bridgeport

Remarks

State Society Delegates to CSMS: Henry L. Fineberg, New York; Robert M. Knowles, Maine; Lloyd A. Hamilton, New Jersey; Theodore H. Lee, New Hampshire

These presentations, if submitted in writing, are published in this issue of Connecticut Medicine.

Reports Of Committees And Divisional Boards

As printed in the Delegate's Handbook, and as supplemented by printed and verbal reports of Divisional Board Chairmen, the reports of all standing and special committees of the Society were accepted by the House.

Election Of Officers And Committees—1964-65

The following slate of officers was elected:

President: Ralph L. Gilman, Storrs

President-Elect: James R. Cullen, Hartford

Vice-President: Orvan H. Hess, New Haven

Secretary: Dennis S. O'Connor, New Haven

Treasurer: Isadore S. Goldberg, Torrington

Speaker of the House: Kenneth F. Brandon, Hartford

Vice-Speaker of the House: Jachin B. Davis, New Haven

AMA Delegate: Ellwood C. Weise, Sr., Bridgeport

Alternate AMA Delegate: Francis J. Kalaman, Norwalk (January 1, 1965-December 31, 1966)

AMA Delegate: Max Caplan, Meriden

Alternate AMA Delegate: Stewart P. Seigle, Hartford (January 1, 1965-December 31, 1966)

Councilor-at-Large: Morris P. Pitock, Bridgeport

Editor of the Journal: Louis H. Nahum, New Haven

Members of Divisional Boards and Committees and others elected or confirmed by the House of Delegates, will be listed in the "Roster" published as a supplement to the August, 1964 issue of Connecticut Medicine.

Presentations And Awards

AMA-ERF: by Dr Pitock

A check in the amount of $7,584 was presented to Arthur Ebbert, Associate Dean of the Yale University School of Medicine, who accepted it on behalf of the School.

CSMS Press Awards: by Dr. Gilman

Press Awards were made as follows:

To Miss Ann V. Masters, *The Bridgeport Sunday Post* (Feature writing).

To Mr. David A. Gibson, *The Hartford Times* (Medical news reporting).

To Mr. Charles J. McGill, *The Bridgeport Post and Telegram* (Editorials).

Past President's Pin: by Dr. Martin

A pin in recognition of his services to the Society as President during 1963-64 was presented to Morris P. Pitock, Bridgeport, by Stevens J. Martin, Chairman of the Council.

Special Award: by Dr. Martin

In recognition of "twenty years of dedicated and superior services to the Society and its members," Dr. Martin presented a bouquet of roses and a cash award to Mrs. Josephine P. Lindquist of the office staff.

Old Business

Report On Hospital Costs And Accounting Procedures

(a) As charged by the House of Delegates on April 30, 1963, the Council filed a report on these matters with the House at this meeting (the report having been prepared by the CSMS Committee on Hospitals).

The Delegates VOTED to accept the Council's report on "Hospital Costs and Accounting Procedures" as an excellent beginning to the study of increasing hospital costs, and requested the Council to continue its study of these matters.

Amendment To The Bylaws Proposed By HCMA

(b) Introduced by the Hartford County Medical Association at the December 11, 1963 meeting of the House, a proposed amendment to the bylaws concerning certain of the censorship powers of the Council was removed from the table to be acted upon.

The Delegates VOTED to adopt the recommendations of the Council that "this proposal be referred to the Council's Subcommittee to Study and Revise the Bylaws in order that the section on censorship may be rewritten as a whole, incorporating all relevant proposals, rather than on a piecemeal basis over a period of time."

Connecticut Medical Service, Inc.

(c) Having received a lengthy report from the Council concerning its unsuccessful efforts to persuade the Board of Directors of CMS to reconsider its unilateral action of January 23, 1964 (whereby the Society was deprived of all rights concerning the nomination of CMS *physician* Directors) and to restore to the Society the exclusive nominating rights which the Superior Court of New Haven County ruled (January 6, 1964) the Society had been entitled to ever since CMS was established in 1948-49, and, having received the reports of recent actions taken by the eight constituent county medical associations relative to this matter (six supported the Council's position and two did not), the Delegates VOTED to adopt a Council-recommend resolution as follows:

A Resolution Concerning The Status Of CMS, Inc. By CSMS, Inc.

WHEREAS: On January 23, 1964, Connecticut Medical Service, Inc. did, in fact, disavow the sponsorship of CMS by the Connecticut State Medical Society, Inc. by amending the CMS Bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society recognize as a fact that, on January 23, 1964, Connecticut Medical Service, Inc. did disavow the sponsorship of the Connecticut State Medical Society, Inc. by amending the CMS Bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., and confirm that, because of this disavowal, sponsorship of Connecticut Medical Service, Inc. by the Connecticut State Medical Society, Inc. no longer exists.

Following this action, a "Statement" was released to the public. The "Statement" described the background, conclusions and significance of the resolution adopted, and will be published in an issue of *Connecticut M.D.* to be mailed out in early May for the information of members of the Society. It is therefore not reproduced herewith.

(d) In a related action, the Delegates VOTED to adopt a second Council-recommended resolution as follows:

A Resolution Concerning Future Sponsorship Of Third Party Agencies By CSMS, Inc.

WHEREAS: Past experience has shown that no satisfactory relationship can endure between the Connecticut State Medical Society, Inc. and third party agencies, such as Connecticut Medical Service, Inc., in the absence of formal legal agreements which stipulate the rights, powers, duties and obligations of each toward the other, therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society, Inc. establish the policy that the Society shall engage in no further sponsorship of any third party agency unless and until there shall exist formal, written, legal agreements between the Society and the third party agency seeking sponsorship, said agreements to specify the rights, powers, duties and obligations of the Society and the third party concerned.

New Business

(a) The Delegates VOTED to adopt a resolution introduced by Michael V. Gualteri, Waterbury, which reads as follows:

SUBJECT: Implementation of Resolution 68 passed by the American Medical Association House of Delegates, June 19, 1963.

WHEREAS: The American Medical Association in session assembled took additional recognition of the "importance of the general practitioner as an essential component of American medicine," and

WHEREAS: Once again recognition was taken of the need for "an adequate number of medical school graduates selecting general practice for their medical careers," and

WHEREAS: The AMA House did resolve to "instruct its Board of Trustees to utilize all facilities at its command to:

(a) Inform the medical schools of the shortage of general practitioners, and request their cooperation in exposing medical students to general practice by lectures, preceptor programs, and

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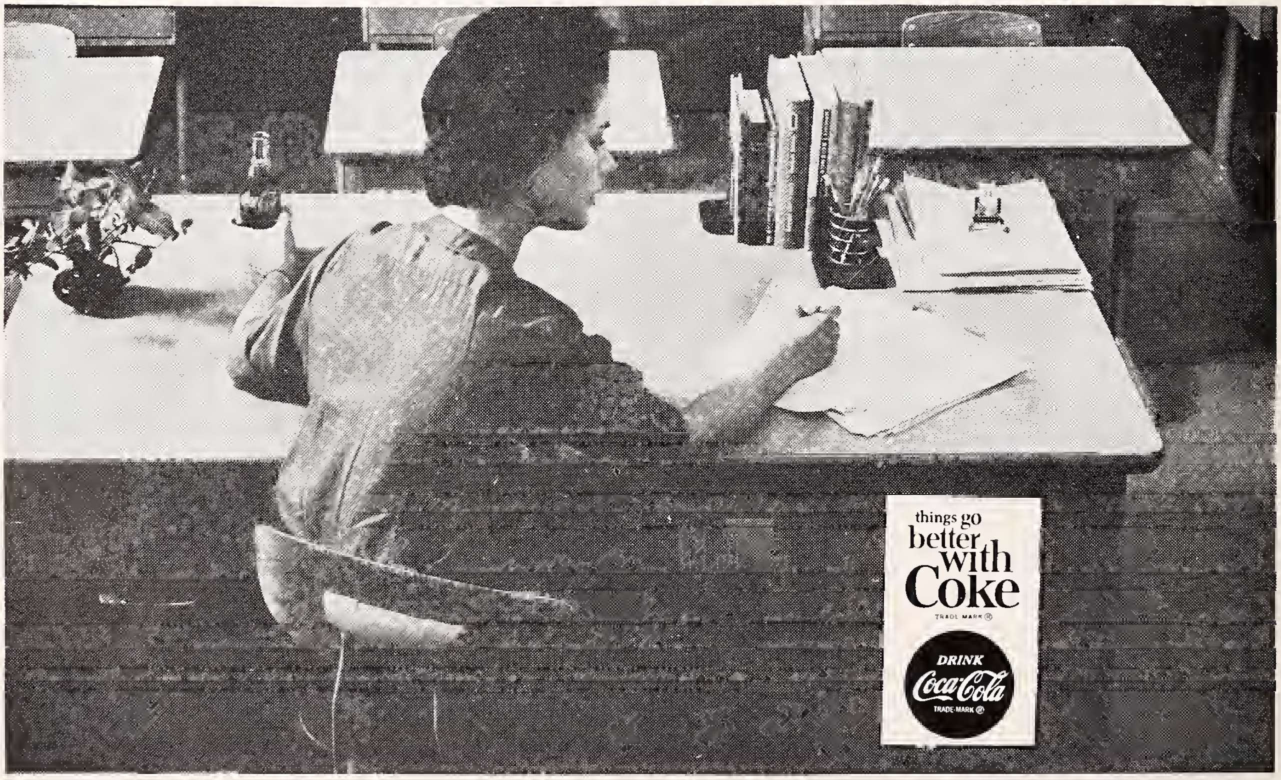

Whether you're a teacher correcting exams. A student cramming for them. A housewife cleaning up after the kids. Or a businessman working late at night. Whoever you are, things go better when you pause and refresh with ice-cold Coca-Cola.

clinical instructors who are practicing general practitioners, and

(b) Inform the constituent state medical associations of the need to emphasize general practice training and to ask these associations' members to encourage students to go into general practice," now therefore be it

RESOLVED: That the Connecticut State Medical Society House of Delegates likewise take cognizance of this problem and instruct our Council to utilize all facilities at its command with deliberate speed to implement the intent of Resolution 68 passed by the AMA House of Delegates, and further be it

RESOLVED: That the Council of the Connecticut State Medical Society report back to the next assemblage of the House of Delegates what actions have been taken in the State of Connecticut and what progress has been made in solution of this serious problem facing the American public, namely, the impending critical shortage of general practitioners to serve the public.

(b) The Delegates VOTED to adopt a resolution introduced by Eugene H. Corley, Bridgeport, which read as follows:

SUBJECT: DISCRIMINATION

WHEREAS: The members of the Connecticut State Medical Society, as physicians, declare there is no foundation or basis in medical science for discrimination amongst the races, and

WHEREAS: The Connecticut State Medical Society takes note that discrimination in the medical profession still exists in the United States, therefore be it

RESOLVED: That the Connecticut State Medical Society go on record as being unalterably opposed to any discrimination in the field of medicine—because of race, creed, color or national origin—whether in patient care, physician opportunity, or professional organization, and be it further

RESOLVED: That the Delegates of The Connecticut State Medical Society introduce this resolution and work to secure its passage at the national convention of the American Medical Association.

(c) The Delegates VOTED to approve a communication to the Belgian Medical Association which had been prepared at the direction of the Council by the Chairman and the General Manager. As with the "Statement" on the sponsorship of CMS, the full text of this communication is being published in an early May issue of *Connecticut M.D.* and is therefore not reproduced herewith.

(d) The Delegates VOTED to adopt the report of Reference Committee "A" (on a resolution introduced from the floor by Edward A. Palomba of Somers) as follows:

BE IT RESOLVED: That the House of Delegates instruct the Council to make what the Council considers to be an appropriate grant (from the Society's general fund) to the Connecticut Medical Political Action Committee (COMPAC) for political education purposes *only*, the making of such a grant to be subject to the opinion of legal counsel.

Unfinished Business

Introduced from the floor by Jachin B. Davis, New Haven, a proposal to amend the CSMS Bylaws was immediately tabled for action at the next meeting of the House. The proposed amendment reads:

IT IS MOVED: That the portion of the CSMS Bylaws concerning a Liaison Committee with CMS, Inc. (Article X, Section 2, Paragraph 1, Line 9) be deleted.

REPORT OF THE SECRETARY

As of December 31, 1963, the membership of the Connecticut State Medical Society totalled 3,473. 185 physicians became new members during the year, but with the loss of old ones through death, transfer and other causes, there was a net gain of only 46 for the twelve month period. As to distribution of member physicians, it is interesting to note that 2,925 live or practice in the three so-called "large counties"—Fairfield, Hartford and New Haven, while 548 are located in the five so-called "small counties"—Litchfield, Middlesex, New London, Tolland and Windham. In the House of Delegates, of course, the number of county representatives directly reflects this numerical and geographical distribution, but in examining the roster of the Council the other day I was surprised to note that Council members from the large counties total 15, while, together, the small county associations hold almost the same number of seats—14. This nearly perfect balance, it seems to me, assures that "the big city fellers" cannot successfully promote points of view which are not also shared by many of those who come from the less populated areas of the State, and that is as it should be.

At the Council meeting of September 27, 1962, it was voted to appoint an Ad Hoc Committee to implement the intent of the following resolution: "That the Council of the Connecticut Medical Society through whatever medium it deems best, immediately direct its attention to an evaluation of the adequacy of the Society's existing Committee and Staff Structure in relation to the increased and increasing responsibility of the Society to its members." Your Secretary was designated as Chairman and was authorized to select members of this committee to include, among others, the General Officers of the Society and the General Manager as consultant. A formal evaluation of this type had last been conducted in 1948 by the Bishop Committee.

In undertaking its assigned task, the Committee elected to limit its study to four main areas. These were: (1) The General Manager's Office, (2) Committees and Divisional Boards, (3) *Connecticut Medicine,* and (4) the Public Relations Department. Subcommittees were appointed by the Chairman to evaluate each of these components and, after receiving the report of the smaller groups, the Committee as a whole formulated certain conclusions which were reported to, and accepted by, the Council. The major recommendations of the Committee have been filed and will not be described in detail at this time. However, several suggestions have already been implemented and are beginning to bear fruit. A thorough study of the public relations operation is continuing and, although temporarily at a standstill because of more pressing affairs of the Society, appropriate recommendations for improvements will be made in the near future.

I have been reading through the committee reports in the "Delegate's Handbook" and note that, as usual, most of our committees are productive. The cumulative work of their members represents a vast amount of dedicated service to their colleagues and an immeasurable amount of time away from practice and family which they contribute gratis to the common good. Would that we had many more like them!

However, I note—also as usual—that an appreciable number of standing and special committees have either no reports to make, or have held no meetings, or both. One of the recommendations made by our ad hoc group last Fall was that a "Committee on Committees" be appointed by the Council to review the Society's over-all committee structure and bring it up to date. Such a body was appointed, and I understand its work was begun several months ago and will continue until this and its related assignments are completed.

On the national scene, as I view it, there is a rather disjointed but imposing effort being made to change the pattern of the present system of American medical care. Literally dozens of pressure groups—some even within, or allied to, medicine itself—are advancing all sorts of proposals and schemes to alter current methods of both providing and financing health services. Each group claims to be motivated only by a desire to do good—to make things better for everybody, but each also calls for one or more drastic changes to be made in our existing methods.

I was reading the other day that the young child is likely to look upon his father's trousers pocket as the source of all good things, because almost every time little junior wants something Dad reaches into that deep and magic cul-de-sac to fish out the wherewithal to buy it for him. Later on, however, it seems the youngster is prone to develop feelings of animosity toward the parent because, as he moves on into adulthood and is mature enough to be expected to face a few of the realities of life, the old man starts to say "no" to his demands once in awhile and then it becomes painfully evident to the growing boy that every well has a bottom. At this point, so the psychologists say, bitter dissatisfaction with the whole new system often causes a serious rift between them which only further maturity—perhaps of both—can heal.

And so it is with our American system of medicine, it seems to me. It is a fine system, because the care patients receive is of high quality and, in almost every community, it is readily available to all. Through the medium of voluntary health insurance the vast majority of our citizens have adequate resources to meet its costs, and the relatively small minority who do not, receive it anyway—at public expense. Most Americans seem to like our system. They are used to it, take its modern medical miracles for granted, and expect it to get even better as time goes on. But, like Daddy's bountiful pants pocket, it will not continue indefinitely as the source of good things—of high quality medical care—if people abuse it; if they can be persuaded that it should all be theirs "for free"; if they can be sold the idea that no matter how often the now healthy body of American medicine could be forced to undergo major surgery it would still remain whole and as vigorous as ever. Some folks simply refuse to believe that a patient can be sick until they see the pathologist's report and, by then, it is often too late to save him.

In blunt terms, what I am trying to say is that if we do not chart and steer the course of medicine ourselves, and take the proper preventive measures, the control of our affairs will be appropriated by others. In contemplating such a happening, let us ponder the significance of the recent so-called "doctors' strike" in Belgium, and the similar major upheaval in Saskatchewan a year or so ago. In both instances, while economic considerations were certainly one part of the picture, the principal inciting factor was political interference with the conduct of medical practice. A similar, though less overt, situation is said to have developed in England under the stringent rules and regulations of the government-operated British National Health Service. The reactions of the professions in these countries and in others suggest that although physicians can become conditioned to being largely deprived of their rightful income, and even to being deprived of much of their freedom as citizens, control and regimentation of medical practice are seldom accepted without a struggle by those who would conscientiously treat the sick.

Government has an undeniable responsibility for meeting the financial aspects of the health and welfare of the indigent and oppressed. In their preoccupation with finding suitable methods to discharge this relatively limited obligation, however, some political officeholders lose sight of that goal and become far more interested in plans for imposing centralized government control on the entire structures of American Medicine than in just providing help for the needy.

It is clear, then, that the leadership of Medicine in these United States—and every one of its practitioners—has a vital stake in the direction in which events move during the years to come. We must be flexible and open-minded in our thinking, and stand ready to seek common ground with all who share our objective of assuring the best possible medical care to everyone, but may differ with us as to how that objective should be reached. Conversely, we must stand firm and united against schemes which we are convinced would destroy the free-choice system that we and our forebears have helped produce in this great country or which would interpose politics and government controls between our patients and ourselves. There is no space to accommodate third parties in the examining room—except for the office nurse!

All of us assembled in this auditorium today are, in one way or another, the leaders of medicine in Connecticut—whether we think we measure up to that grave responsibility or not. In my judgment, therefore, all of us together would do well to personally seek out our 3500 colleagues in every part of the State and—in the words of the late President—say to them: "We need your support. Give us your help."

Respectfully submitted,

Orvan W. Hess, M.D., *Secretary.*

REPORT OF THE COUNCIL

Mr. Speaker, Mr. President, Members of the House, and Distinguished Guests:

Since I last reported to the House of Delegates on December 11, 1963, there have been five meetings of the Council at which an average of 22 out of a possible 29 members have been present. This fine record of attendance, I feel, speaks well for the dedication of the men who have been asked by their colleagues throughout the State to transact the business of organized medicine in Connecticut from month to month—and, sometimes, even from week to week.

As at every convening of this body during the past six years, the Chairman of the Council must once again inform you that dealing with the Society's relationships with Connecticut Medical Service, Inc. has taken up an inordinately large part of our time and, in fact, will constitute a principal item in my review of the Council's recent activities today. I warn you in advance that it will be necessary for me to dwell at considerable length on that one subject and I ask each of you to give these important matters the benefit of your fullest attention and call upon you to use your very best judgment in taking whatever actions seem most appropriate to you at the proper point in the Agenda.

Before moving into the CMS question, however, I will bring you up to date on a number of matters of unfinished business of the House as well as one or two matters not previously brought to your attention:

(1) *The Relative Value Study:* During the past six years, a great deal of time and effort—and a considerable amount of money, too—have been put into this project by a Committee under the Chairmanship of Dr. Benjamin D. Thaw of Hartford. Several of our insurance study groups—the Committee on Third Party Payments and Dr. Bradley's Ad Hoc Committee to formulate new and better prepayment methods—have recently informed the Council that a Relative Value Scale (or Index) would be most helpful to them in their work; that, indeed, they consider it of the utmost importance that one be derived from the work already done at the earliest possible time. Dr. Thaw now finds it impractical to devote the time to this assignment which he feels is necessary, and Dr. Stewart P. Seigle of Hartford has only last week agreed to take over as chairman of the Committee on Relative Value Study. With Dr. Thaw's assistance, and the acquisition of certain specialized personnel to perform some of the more technical work remaining to be done, we are hopeful and optimistic that the House will receive a final report on this important undertaking at its next session in the Fall.

(2) *The Corporate Practice of Medicine:* Dr. David A. Grendon of Sharon and his Ad Hoc Committee on Corporate Practice have continued to investigate all aspects of the Outpatient Rider still being sold by Connecticut Blue Cross—and still making payments to hospitals for the services of doctors of medicine. Just what steps it may prove desirable or practical for the Society to take in pursuing this matter to a reasonable conclusion are not known at the present time, but we are being constantly advised by competent legal counsel and will base our final decision on whatever recommendations he makes to the Council through its Ad Hoc Committee. As in dealing with so many problems facing medicine today, the basic question here seems quite simple but the answers are likely to prove quite complex.

(3) *The Society's Committee on Staff Structure and Function:* An Ad Hoc Committee, under the chairmanship of Dr. Orvan W. Hess of New Haven, continues its studies relative to improving the efficiency and effectiveness of the Society in its service to its members and to the public. Since Dr. Hess has described at some length the work of his committee, in his report to you as Secretary, I will not enlarge further upon this activity of the Council.

(4) *Kerr-Mills in Connecticut:* As I hope all of us appreciate, the physicians of the State may have a great deal to lose if the Kerr-Mills (Medical Assistance for the Aged) program in Connecticut does not do the job for which it was intended, or does not do the job well enough. Commissioner of Welfare Shapiro and his Medical Director, Dr. Edwin R. Connors, have been most cooperative with and informative to representatives of the Council who have met with them several times during the past two years. We have also learned much from a group of our general practitioners and from other sources concerning certain deficiences in the program that may be preventing it from achieving a full realization of its purposes. At the next session of the General Assembly, which opens next January, it will be necessary for our legislative people to appear in support of amendments designed to improve the operation of MAA from the administrative and financial standpoints. In the final analysis, however, none are so well qualified to report on the merits and inadequacies of the plan as the hundreds and hundreds of our members who are learning how MAA works at the point of delivery—at the grass roots level, where the patients are. Without suitable stimulation, the General Assembly is likely to deal only with the centralized aspects of this "Aid to the Aged"—the funds to be appropriated, liberalizing the eligibility requirements and so on. But if there are troublesome problems complicating matters for doctors and their older patients out in the field, then it is incumbent on those doctors to inform the Society of the difficulties they are encountering, and, further, to be willing to come forward at Hartford next Spring and bear personal witness to the things about the MAA program they have found wanting. As we all know, the most convincing testimony at any hearing is that which comes from experts—in this case, the practicing physicians of the State.

(5) *Amendments to the Bylaws:* At the last session of the House, a proposed amendment defining the various categories of disciplinary actions the Council might take against erring members was referred back to the Council's Subcommittee to Study and Revise the Bylaws for further review and report. At that same meeting, an amendment was introduced by the Hartford Association concerning the powers of the Council as the Board of Censors of the Society, particularly with respect to its latitude and limitations in ruling on appeals from disciplinary decisions of the constituent county associations. Today, the latter proposal will be taken off the table for action by the House, and the Council recommends (3/25/64)

that you vote to refer it to the Council's Subcommittee to Study and Revise the Bylaws in order that the section on censorship may be rewritten as a whole, incorporating all relevant proposals, rather than be amended on a piecemeal basis over a period of time. The Council is hopeful that you will find merit in this recommendation, and see fit to adopt it at the proper point in the agenda.

(6) *Report on Hospital Costs and Accounting Procedures:* A year ago, the House charged the Council with making a study of rising hospital costs and the accounting procedures used by the general hospitals throughout the State. The Council promptly "farmed out" this assignment to our dedicated Committee on Hospitals and its seemingly tireless chairman, Dr. Leopold M. Trifari of Hamden. On April 22nd, the Committee submitted its report on these matters to the Council and, having been approved by the Council, it is before you today with the recommendation of the Council that it be similarly approved by the House. I should like to make an additional personal recommendation that if the report *is* approved, your action include commendation of the Committee on Hospitals for the excellence of its work, and your authorization for the report to be published in *Connecticut Medicine* for the enlightenment of all our members. I had thought to bring to your attention a number of excerpts from the report, but since I am told that each of you will receive a mimeographed copy of it at the convening of this meeting, I urge you to read it through before this afternoon's session in order that you may be fully aware of its content prior to taking action on the Council's recommendation that it be approved.

(7) *Cigarette Advertising in Connecticut Medicine:* In keeping with the Resolution on cigarette smoking adopted by the House last December, the Council reviewed its position with respect to accepting cigarette advertisements for the Journal. Although the decision on this question was far from uananimous—and despite the fact that both our Treasurer and Editor will inform you that we can ill afford to lose even a penny's worth of advertising revenue in our principal publication—the majority of Council members felt that, to be consistent with the Society's official position on the hazards of smoking to health, this exclusion should be made.

(8) *Committee on Health Careers:* Under the able direction of Dr. Bernard F. Mann, Jr. of New Haven, the Committee on Health Careers has continued to develop its recruitment program among the public and private schools throughout the State, and has received substantial and rewarding cooperation from members of the Woman's Auxiliary in many of the county areas. At present, the Committee is considering the merits of forming a "state association on health careers," which would coordinate the efforts of many voluntary agencies in Connecticut that have an interest in attracting qualified young people into the medical and paramedical professions, and would avoid a great deal of duplication of effort in achieving their single goal. In keeping with a national trend in this direction, the Council has authorized Dr. Mann to pursue a possible amalgamation of interested agencies, with the understanding that, if approved, financial support of such an association by the Society is implicit, and with the reservation that involvement of the Society in such an arrangement would have to be spelled out in writing in order to avoid future difficulties regarding the rights, powers, duties and obligations of the Society and the other participating agencies. We will await a later report from Dr. Mann and the Committee on this project.

(9) *Reports of Council-Appointed Representatives and Advisors:* A number of annual reports have been received from individuals and committees appointed by the Council. These are printed in your Handbook. Since none of them contain recommendations, the Council recommends that they be accepted as printed unless the House is otherwise disposed in regard to a particular report.

(10) *Report of the Nominating Committee:* Printed in your Delegate's Handbook is the complete slate of officers, committees and appointees nominated by the Council for election or confirmation at this meeting. I will present the slate in detail at such point in the agenda as this report comes up for action. At this time, however, I would direct your attention to the "package" of supplemental materials you received upon registering and, specifically, to the "Note" at the bottom of the front page. There we have listed several changes in the slate printed in your "Handbook." The changes were made necessary by the deaths of the members originally nominated. I can report to you that the slate, and all nominees on it, represents the carefully chosen selections of a majority of the members of the Council.

(11) *Communication to the Physicians of Belgium:* At the April 22nd meeting of the Council, it was voted to direct the Chairman and the General Manager to draft an appropriate communication to the leadership of the Belgian doctors which, if approved by this House of Delegates, would convey to our colleagues across the sea a measure of our identification with their cause without necessarily endorsing the course of action they felt it necessary to take recently to preserve their personal and professional freedom. A draft of such a letter is attached as Item No. 3 in the package of supplemental materials I referred to a moment ago. The decision in this matter rests entirely with the House, of course, but it is my personal feeling that the precise wording of this draft makes its message worthy and meaningful but avoids saying anything that is better left unsaid. It would be my hope that if it is approved by the House at all—in the present or amended form—it will be approved without an appreciable number of dissenting votes. Anything short of that, it seems to me, would tend to largely defeat its purpose. I might add, incidentally, that the stimulus for this recommendation of the Council came from one of our Danbury members—Dr. E. Lloyd Dawe—who, himself, has had extensive first-hand experience in jousting with bureaucrats under the British variety of government-controlled medical care.

(12) *Connecticut Medical Service, Inc.:* Before embarking on the report of the Council concerning the situation as it now exists in the longstanding controversy between the Society and CMS, I want to say to you that I know of not one member of the Council—indeed, not one member of the Society—who I have any reason to think will derive the least satisfaction from the course that recent events have taken. If there are physicians in the State who have been motivated by a desire to bring about the present impasse—and I have heard this allegation, from time to time—I can report to you in all candor that I have not run across them and, as far as I am concerned, none such has brought any influence to bear on the decisions of your Council. Following the December meeting of the House, Judge A. J. Coles, of the Superior

Court of New Haven County handed down a "Memorandum of Decision" in our litigation with CMS on the 6th of January. His four principal rulings were as follows:

"It is adjudged: (1) That the petitioner Jachin B. Davis is a member and director of CMS with full voting rights, filling the unexpired term of Dr. Frank Polito (resigned), and that he became so on December 19, 1962 when he was nominated by the Council of the Medical Society; (2) That the petitioners Dr. Max Caplan and Dr. Howard K. Ente are members and directors of CMS, with full voting rights, for two-year terms commencing on February 19, 1963; (3) That the respondents, Dr. Israel E. Blodinger and Dr. Frank H. D'Andrea are not members and directors of CMS; (4) That there is no agreement between the Medical Society and CMS concerning the selection of the physician members (Corporators) of CMS."

On January 22, 1964, the Council met to consider the significance of Judge Coles' "Memorandum," and what steps could be taken to reestablish contact with the Board of Directors for the purpose of attempting to work out some alternative method for selecting the physician Directors of CMS which would be satisfactory to both parties, it being evident that the prior arrangement was no longer agreeable to the Board. At this meeting, it was reported that the Directors were to meet on the following date for the express purpose of amending the CMS bylaws so as to deprive the Society of its traditional right to name the physician members of the Corporation. In an effort to forestall this action by the Directors, the Council had hand-delivered to the CMS building on the afternoon of January 22nd a series of resolutions which, in essence, pleaded with the Corporators *not* to make any precipitate decisions concerning the bylaw amendment until both sides had had an opportunity to talk over the situation through the established liaison mechanism, and determine whether some accommodation of divergent views could not be reached *before* drastic changes in the bylaws were made. I trust all of you have read the minutes of the Council meetings held during January and February of this year, and the comprehensive "Summary of Events" which was mailed out to all our members on February 26th. In any event, I wish to emphasize the fact that the majority of Directors completely ignored the requests of the Council; they completely ignored the pleas of five of their physician Directors that they exercise forbearance; and proceeded forthwith to amend the bylaws as planned.

Then—and then only—did they approach the Council with the olive branch of peace extended, and suggest that we might get together sometime soon to try to work out a new system of nominating procedure.

From that time—January 24th—until this very moment, the Council and its legal advisor, Mr. Grant Nickerson, have made every effort to come to an agreement on the major question presently at issue—how the physician Directors of CMS are to be selected. In all the negotiations which followed, the Council laid down only one "minimum requirement" which had to be met by the Board; i.e., that no matter what alternative method of nominations was arrived at, it must again assure that "the physician Members of CMS, Inc. (will) be chosen from among those designated by the Council of the Connecticut State Medical Society."

On March 23rd, after much preliminary study by respective legal counsel and others, a joint meeting of the Liaison Committees of the two Corporations was held. At this meeting, a number of prepared drafts of documents were reviewed: "A Statement of Joint Understanding, 1964—CMS-CSMS," which outlined in general terms what each corporation could expect of the other as to rights, powers, duties and obligation; A "Letter of Intent," which, if all else could be agreed to, the President of CMS would send to the Chairman of the Council, and the Chairman would acknowledge acceptance by the Society of the terms stated in the "Letter"; and, finally, a proposed amendment to Article I, Section 1 of the CMS bylaws which read as follows:

> The President shall appoint a Nominating Committee composed of two physician Members and two lay Members who shall make all nominations for membership in the Corporation. At least three months prior to the Annual Meeting of the Corporation, the Nominating Committee shall solicit proposals for physician-Members from the Council of the Connecticut State Medical Society. If any physician is proposed for nomination by the Nominating Committee other than those proposed initially by the Council his name shall first be submitted to the Council, and if within thirty days thereafter the Council notifies the Committee in writing that such proposed nominee is not acceptable to it, that person shall not be nominated.

The liaison meeting lasted nearly five hours and a free and open discussion was held on all matters relative to the content of the drafts of the three documents just described. I think it fair to say that there was no serious disagreement in any quarter as to the general terms and conditions outlined in the "Statement of Understanding" or the "Letter of Intent." A few minor changes in wording were approved, and it was voted to refer these two documents to the Council and to the CMS Board for disposition. In the matter of the proposed amendment to Article I of the CMS bylaws, however, there was strong and divided opinion as to the section on the method of selecting physician candidates for nomination to membership in the Corporation. All members of the CMS component appeared to find the proposal to their liking and gave it their approval. On the Council side, there was general agreement that the proposal did not restore nominating rights to the Council as they had existed before the bylaws were changed, but at least three members of our component said they felt it to be an acceptable compromise. Since there appeared to be no way in which the liaison group could accommodate this divergent point of view to any greater extent, it was voted to transmit this document also to the two parent bodies for disposition. After considerable discussion, the CMS group then agreed to restore the so-called "recall" provision to the bylaws in pretty much its old form; i.e., for stated cause, sustained by a two-thirds vote of all voting members of the Council, the resignation of a physician Director would be demanded by the Board. Everyone appeared to find this proposal acceptable.

Just prior to the adjournment of this meeting, your Chairman pledged to the assembled group that he would bring these matters to the Council for action two days later, on March 25th; that he would furnish each member of the Council with printed copies of all three documents, as amended; and that he would ask each member of the CSMS liaison component to express his individual views on all points at issue. In turn, Mr. Coolidge clearly gave the meeting to understand that *he* would call a meeting of the Board of Directors at an early date for an identical purpose. When the meeting broke up, it was also clearly understood that because time was a factor—the House of Delegates meeting being only about four weeks away—each side would move promptly to arrive at final decisions at the earliest date possible. This point was given particular emphasis on the grounds that should additional liaison sessions be required, as much time as possible should be allowed in which to hold them.

On March 25, your Chairman carried out his pledge to the letter. The Council received every bit of information concerning the liaison meeting and about the documents presented that could be conveyed to it by its liaison representatives. After a full and extended discussion of the proposed bylaw amendment on nominations, a motion to accept the proposal was lost by a roll-call of 15 nays-8 yeas. The consensus of the majority was that the amendment gave no written assurance to the Council that any of its selections would be elected as Directors, or even nominated for same, and that it therefore failed to meet the Council's "minimum requirement" in this regard, stated a moment ago. In this consensus, legal counsel concurred.

Thereafter the members voted 20-2 to inform the Board of Directors that the Council was "unwilling to consider any restoration or continuation of sponsorship of CMS by CSMS which does not provide for amendment of the CMS Bylaws to restore the complete freedom of the Council to select and recall physician members of CMS, as that privilege existed prior to June 6, 1963; that if agreement on this point is to be resolved with CMS, it must be accomplished by April 8, 1964; and that, if no such agreement is reached by that date, the Council re-affirms its intention, expressed on February 15, 1964, to recommend to the CSMS House of Delegates (today) confirmation of the fact that sponsorship of CMS by CSMS no longer exists."

Notice of this action was forwarded by letter to the CMS offices in New Haven on the following day, March 26th. From then until the 9th of April, nothing was heard from Mr. Coolidge or from anyone else connected with the Corporation. On April 9, a letter was finally received from the CMS President which read, in part: "It was understood at the (liaison) meeting of March 23, 1964 that this mutual agreement would be recommended to the Council and the CMS Board for approval. The fact that the Council disapproved the agreement at its meeting two days later eliminated the necessity for calling a special meeting of the CMS Board to approve the agreement."

After consulting with legal counsel, and being deeply concerned that no real reply at all might be forthcoming from the Board of Directors prior to this meeting of the House, I wrote to Mr. Coolidge on April 13, informing him of my concern that no meeting of the Board had been called or apparently would be called by him, and stating: "I am unable to determine from your letter of April 9th whether you intend to submit these important questions to the CMS Board of Directors for final decision by *all* the Directors, or whether I am supposed to report to the Council as final your (own) stated opinion that the necessity for calling a special meeting of the Board has been eliminated. . . ." I further informed Mr. Collidge that, if the latter were the case, I was sure "the members of the Council would be greatly disappointed to learn that the Board of Directors had not been given an opportunity to act (formally) on any and all of these matters," and that I felt that "at least one stone would have been left unturned if either our House of Delegates or your Board of Directors had not fully and finally addressed themselves to answering every question that has been raised."

Four days later, on April 17th, Mr. Coolidge replied, again going into great detail about what he still referred to as the "agreements" reached by the liaison representatives at the March 23rd meeting, and stating that he was at a loss to understand "why the Council was unwilling to accept the recommendations of its own Liaison Committee." Let me reiterate, at this point, that our Liaison Committee with CMS is a fact-finding body *only,* not authorized to make any "agreements" with anyone, and that the recommendations of each individual member of the Liaison Committee with CMS were filed with the Council on March 25th. At any rate, Mr. Coolidge informed me that this whole matter was going to be taken up at the next regular meeting of the Board of Directors on April 23rd.

Before disclosing to you what I believe to be the final chapter in this long and frustrating exchange, I wish to make special note of the fact that, on two occasions during the months of January and February, a meeting of the Council was called with only forty-eight hours notice and that these meetings were held, respectively, on a Saturday and on a Sunday. I am proud to report to you that, even with such brief notification, at least nineteen members of your Council gave up their weekend relaxation to attend both meetings, and that none of them left either session until all business was completed. To me, this is a measure of the sincere dedication your Council representatives have to protecting the proper interests of every member of this Society and of the public as well.

But on April 23rd, I am reliably informed, at the "regular meeting of the Board" to which Mr. Coolidge referred in his last letter, less than a quorum of the CMS Directors showed up and, as a consequence, no business whatever could be transacted. So at this writing, it appears that at least one-half of the Board members are content to let this conroversy be settled without benefit of their advice or judgment. I leave it to you to draw your own comparisons between the performances of the two groups in attempting to resolve our differences.

It is clear, then, that there exists today a complete impasse between CMS and the Society concerning the terms of their relationship. In this necessarily long and detailed account of all that has transpired in the past four months, I have referred to many actions taken by the Council and by the Board, and to a number of letter in cross-correspondence which have been sent back and forth at various times. I have most of the supporting materials here with me and, at the proper place on the Agenda, I will be pleased to read to you verbatim any or all parts of them in accordance with your wishes. Also, our legal advisor will join us later to try to answer any questions you may desire to ask of him.

Your Council has acted conscientiously in your behalf, and its consensus of opinion is that since the Society is no longer to be granted any meaningful choice in the selection of the physician Directors of CMS or any meaningful voice in guiding its future medico-economic policies, the phrase "Sponsored by the Connecticut State Medical Society" is no longer either warranted or appropriate with reference to Connecticut's Blue Shield plan. Therefore, as first adopted on February 15, 1964, and as re-affirmed by a roll-call vote of 18 to 4 on April 22, 1964, the Council recommends for your adoption today a resolution titled: A Resolution Concerning the Sponsorship Status of CMS, Inc. by the Connecticut State Medical Society, Inc." You all have a printed copy of this resolution in the package of materials you received upon registering. I shall read it now:

Whereas: On January 23, 1964, Connecticut Medical Service, Inc. did, in fact, disavow the sponsorship of CMS by the Connecticut State Medical Society, Inc. by amending the CMS Bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc., therefore be it

Resolved: That the House of Delegates of the Connecticut State Medical Society recognize as a fact that, on January 23, 1964, Connecticut Medical Service, Inc. did disavow the sponsorship of the Connecticut State Medical Society, Inc. by amending the CMS Bylaws so as to deprive the Society of its right to name the physician Members and Directors of CMS, Inc. and confirm that, because of this disavowal, sponsorship of Connecticut Medical Service, Inc. by the Connecticut State Medical Society, Inc. no longer exists.

Beyond the recommendation of the Council concerning this resolution, I will report to you also on the related actions taken by our constituent county associations at their recent annual meetings. In the counties of New Haven, Fairfield, Litchfield, Middlesex and Tolland, the memberships voted to support the position of the Council embodied in the resolution before you. The Board of Directors of the Hartford Association similarly voted to support the Council's position at its meeting on April 22nd. However, the memberships of the associations in New London and Windham counties have voted not to support this position and expressed their desire that sponsorship of CMS by the Society continue. Since not all the associations took *identical* actions in this regard, I will ask the Speaker to allow a representative of each county group to clarify the action of his group, should each county wish that to be done.

On February 15th, the Council also voted to recommend adoption by this House of a second resolution, which is titled: "A Resolution Concerning Future Sponsorship of Third Party Agencies by the Connecticut State Medical Society, Inc." In the interest of conserving time, I will defer reading this resolution until it is taken up under "New and Unfinished Business."

There have been many side-issues raised in this controversy with CMS which the Council has weighed and found to be without merit. For example, in his statement to the Corporators of January 23rd, Mr. Coolidge contended that the original method of naming the physician Directors unfairly gave the Council-appointees the power to pick and choose their lay fellows on the Board, and yet the record of fifteen years shows that *only physician nominees* have ever failed to be elected to membership in the Corporation. He further contended that this same former nominating procedure gave the Society—and more specifically, the Council—the ability to control "the election of the officers (of CMS), the composition of its committees, and the determination of its policies," and yet he did not and, in fact, *could not* offer a single historical fact to back up this contention. The Council has not been distracted by the raising of such diversionary issues, and I am hopeful that the House will not be diverted by them either.

In conclusion, let me express my gratitude for having been given the honor and privilege of serving the members of the Society in our continuing efforts to assure a high quality of medical care and health services to all the people of this State, and to preserve the maximum degree of freedom of professional judgment for all its physicians. I have been only the elected *spokesman* for the Council, however, and what has been achieved during this past year represents the combined and unselfish efforts of our President, Dr. Morris P. Pitock, and his fellow state officers, the eighteen other county-appointed Councilors, a large number of dedicated committee people and the loyal and hardworking members of our office staff.

Respectfully submitted,

Stevens J. Martin, M.D.
Chairman of the Council

REPORT OF THE GENERAL MANAGER

Mr. Speaker, Mr. President, members and guests
of the House of Delegates:

Having been given the privilege of reviewing with Dr. Martin beforehand the manuscript of the superb and comprehensive "Report of the Council" he has just delivered to you, I did not have to be told that any offering I might make at this point would be more than a little anti-climactic. Hence, I have prepared no formal report for today's meeting and have none to submit.

But the other day, I ran across a little news item in the back pages of the *The New Haven Register* which rubbed me very much the wrong way and, by sharing it with you, I hope to get rid of some of the shock and anger the article engendered in me..

It seems that the New York State Department of Education has ruled that a public school pupil *must*—yes, *has to*—salute the American flag in class unless he declines to do so for religious reasons. Legal counsel for the Department says that a local school board may require—can actually *insist on*—a recitation of the Pledge of Allegiance by students at the morning assembly.

The issue here was raised by a report from one of the State's suburban high schools that twenty students have been refusing to salute the flag for more than a month now. Their reason? They claim that recitation of the Pledge violates the First Amendment to the Constitution, and places in jeopardy their guarantees of freedom of religion and of speech and of the press and so on. One particularly vocal young non-conformist says he positively won't participate in such a ceremony "until he can salute a flag that will fly over the entire world," and there is even some talk that the dissenters may carry their protest all the way up to the Supreme Court for a decision—that's how strongly *they* feel about it.

It is often said that we are living in a rapidly changing world; that we must learn to adapt ourselves to new ideas and new ways of doing things. I guess that's the way it is, and probably that's the way it has to be. But just for old-times' sake, and to help keep alive and meaningful a tradition cherished by our generations of Americans, may I ask all of you who still look upon our Constitution as an instrument of freedom—not one of prohibition or coercion—to rise now, face the flag, and join me in pledging our allegiance to the Stars and Stripes.

I pledge allegiance to the flag of the United States of America, and to the Republic for which it stands; one nation, under God, indivisible, with liberty and justice for all.

Thank you.

William R. Richards, M.D.
General Manager

ADDRESS OF THE INCOMING PRESIDENT

Mr. Speaker, Officers, Members of the House of Delegates and Guests:

The honor of being President of the Connecticut State Medical Society comes to relatively few and it is even less common for it to be conferred on a rural practitioner in the northeast area of the state. Hence I am doubly appreciative of this honor, and I shall try to discharge the duties and responsibilities of the office in keeping with the example and tradition of the long line of my illustrious predecessors.

I have served on the Council for some eleven years and have observed and participated in, to some extent, many activities of the Society. During this time we have had numerous serious problems with which to cope, both within our own family and also in our relationship to other organizations. We have seen many changes, even in this short space of time, in the practice of medicine and in the methods of financing medical care. I see no cessation of these problems in the forseeable future.

There is the problem of increasing specialization and the decreasing number of recent graduates who elect to go into what, for want of a better term, is labeled general practice. There are even changing concepts of what constitutes general practice. There is very much to the fore the question of house staff for the community hospitals and the seeming monopoly of the available candidates by university connected hospitals. Add to these the increasing centralization of medical care in hospitals and what, to many, seems to be the increasing intrusion of the hospital itself into the actual practice of medicine, and we have quite a list of serious problems requiring sound reasoning and statesman-like consideration for their solution.

Then there are all the problems of third party payments for medical care—be they government, insurance companies, or Blue Shield plans. Labor and management are increasingly pushing for full coverage of all, or nearly all, medical services. The general public has become much more sophisticated insurance-wise and more and more it wants its medical care insurance to pay the whole bill. All of these socio-economic forces, to say nothing of all the political pushing and pulling that has become inextricably involved in these questions, will require many hours of study and discussion on our part. We cannot afford to let them be resolved without our active participation. Neither can we afford just to oppose changes because they are not exactly what we have been accustomed to doing.

Your officers and councilors assume a very heavy burden in conducting the affairs of the Society. They devote many, many hours and travel many miles in discharging their duties—all of which means a not inconsiderable financial sacrifice on their part. Many times we have been criticized for the decisions we have made or the policies we have adopted. Occasionally we are given a pat on the back. However, as we have gone around the state to attend the county meetings, and have conversed with colleagues at staff meetings or in the coat rooms, we have been impressed—at times even disheartened—by the widespread lack of knowledge on all these problems. Even more discouraging is the seeming apathy of large numbers towards them; the feeling that the government is inevitably going to take over so why bother to fight it; the strange belief that we shall be free to practice just as we always have when this occurs, and many similar ideas. As your President I say to you: shake off this apathy—become informed—discuss these questions with your colleagues—attend your county meetings and participate in the discussions—do not be influenced only by the few who may be most vocal in these matters—let your councilors and delegates know how you feel and what you think they should do. Only in this way can your officers and the Council truly represent the majority opinions of a strong, united profession—and a strong united profession is sorely needed in these times.

All that I have said so far will appear on the President's Page in *Connecticut Medicine* in May. I have addressed these remarks personally to you today because you are the leaders of our Society in your county associations and local societies. You are, or should be, the ones best informed since you regularly get the minutes of the Council meetings. You are, or should be, the ones to spread the information to your colleagues, to discuss these questions with them, to stimulate them to attend meetings and make their views known. You are, or should be, the ones to assess what policies the membership at large really wants to have adopted so that you can truly represent these views in your deliberations in this House. No one expects unanimous agreement on all issues—doctors are too much individualists for that—but we should strive to pursue courses of action that we feel will have the solid support of a large majority of our members. As you deliberate and act on the important items on your agenda at all sessions, ask yourselves "is this course of action what the majority of our members really wish; is it for the best interests not alone of ourselves, but even more importantly, is it for the best interests of our patients and the profession of medicine generally?"

Ralph L. Gilman, M.D.
President

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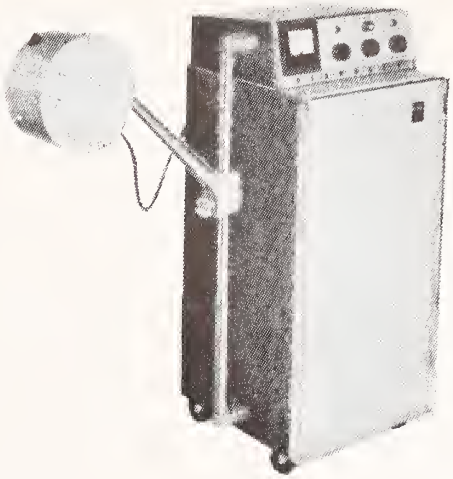

DOCTOR

Transcripts of the Diapulse Symposium held at St. Vincent's Hospital, Bridgeport, Conn., April 22nd, 1964, will be made available to all Medical Doctors who ask for the "Diapulse Story."

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AROUND THE STATE

Hartford County

The Woman's Auxiliary to the Hartford County Medical Association celebrated its Twentieth Anniversary with a gala birthday party held at the Hotel America, on April 28th. A "Sing-Along," with original lyrics by Mrs. Otto M. Hirschfeld, outgoing vice-president in charge of program, were led by Edythe Spekter, and Irene Kahn of the Hartt School of Music. About 130 attending members joined in the song, which was set to the tune of "Memory Lane," which was the theme of the afternoon, in honor of the past-presidents.

A biography of each of the past presidents was read by Mrs. Forrest Gibson, incoming president, and the birthday cake was cut by Mrs. Paul S. Phelps, the oldest living president.

The following officers were installed:

Mrs. Forrest D. Gibson, President
Mrs. David Waskowith, President-Elect
Mrs. J. Howard Johnston, First Vice-President
Mrs. Edmund Beizer, Second Vice-President
Mrs. Gerald V. Levreault, Corresponding Secretary
Mrs. Robert H. Campbell, Recording Secretary
Mrs. Edwin R. Connors, Treasurer
Mrs. Edwin McCloskey, Assistant Treasurer

News From Yale University School Of Medicine

A grant of $100,000 has been awardeed to the Yale School of Medicine by The Burroughs Wellcome Fund of Tuckahoe, New York, to support a Section of Clinical Pharmacology under the direction of Dr. Paul Calabresi, Assistant Professor of Medicine and Pharmacology.

Receipt of the award was announced recently by Dr. Vernon W. Lippard, Dean of the School. The grant, which runs for five years, is given specifically to support Dr. Calabresi's work in directing a program of teaching, training and research in clinical pharmacology.

According to William N. Creasy, President of the Fund, the purpose of the grant program is "to assist medical schools in providing laboratories and clinics where students may learn under a first-class scientist and teacher to apply basic scientific knowledge and techniques to the study of clinical pharmacology, and to develop thereby clinical investigators who are capable of evaluating critically the therapeutic efficacy and mechanisms of the actions of drugs."

Yale's Section of Clinical Pharmacology, established a few years ago, operates with the active support and collaboration of the Departments of Internal Medicine and Pharmacology.

New Haven County

Board Of Governors Meeting New Haven County Medical Association

April 23, 1964

The first meeting of the Board of Governors of the New Haven County Medical Association and its newly elected officers was held at the Colonial House, Hamden, Conn. on Thursday, April 23, 1964. Dr. Jack Galen, Derby, was elected Chairman of the Board to preside over the year 1964-1965.

Since this was the last meeting that Dr. Jachin B. Davis will attend as our Councilor, the Board, by a rising vote of thanks, paid tribute to the monumental work Dr. Davis has done County and State-wise to further the interests of the physicians as an individual and to organized medicine. His presence in his new office will still be felt in the Council and we look forward to his visits with us as an Honorary Guest.

The Agenda provided free and open discussion. The question of Third Party complaints about overcharges was thoroughly aired. Dr. Louis Backhus of Waterbury, cautioned the Board to tread slowly, citing the instance of a suit being brought by an Ohio physician against his county medical society for $1,100,000 for harm done by publicity resulting from a decision of their Board that he had overcharged a patient. This was later reversed by a court of law which found the doctor entitled to his fee.

Matters pertaining to the meeting of the House of Delegates which is to be held in Hartford on April 28th were reviewed with an eye to appropriate action.

The meeting was followed by a social hour and dinner at which time Dr. Max Caplan, Meriden, as a director, reported the meeting of the Board of Directors of C.M.S. held that afternoon. It was obvious from his remarks there can be no rapprochement at this time.

H. A. Levin, M.D.

Letters To The Editor

To the Editor:

Connecticut Medical Service, Inc. is no longer sponsored by the Connecticut State Medical Society because the CMS Board of Directors voted (1/23/64) to deprive the Society of the right to name the eight physicians who make up one-half of the sixteen members and directors of the Corporation. Many of my colleagues hereabouts have been asking me about continuing their status as CMS Participating Physicians and, while I recognize that each practitioner must make this determination for himself, I have answered all these inquirers by letting them read a letter similar to the one I wrote to CMS recently which explains the reasons for my own decision in the matter. For the information of other members of the Society, I ask that you publish the foregoing and the following in "Letters to the Editor" section of the next issue of CONNECTICUT MEDICINE.

"Mr. John Coolidge, President
Connecticut Medical Service, Inc.
Post Office Box 1415
New Haven, Connecticut
Dear Mr. Coolidge:

The Blue Shield system of prepayment is intended to be a mechanism for cooperation between doctors and their patients to provide for efficient, economical and equitable financing of physicians' services, particularly for patients of low or modest income. Inasmuch as physicians actually underwrite such plans, they should be granted a major voice in their operation and, in most parts of the country, this is the case. I believe wholeheartedly in the Blue Shield system, and have supported our state Blue Shield plan for many years.

In my judgment, however, the present directorate of Connecticut Medical Service, Inc. has decided, very unwisely, to deprive both physicians and patients of their rights as equal partners in the future development of the plan, and has thereby converted CMS into a wealthy, self-perpetuating, independent agency for the disbursement of money rather than for guaranteeing the provision of medical services to a limited segment of the public which needs doctor-subsidized care.

As a Participating Physician, I have been a staunch (if sometimes critical) supporter of CMS since its inception and, on this account, I am loathe to withdraw my support from what should be—but no longer is—an excellent and unique mechanism for service to the Connecticut public. But, if by July 1, 1964, the Bylaws of CMS, Inc. have not been amended to provide that *more than 50%* of the CMS Board of Directors shall be Participating Physicians selected by the Connecticut State Medical Society, I hereby serve notice that, sixty days after July 1, 1964, the agreement of participation between the Corporation and myself is to be completely and finally dissolved.

I wish to add, however, that if the conditions outlined above are met by the Corporation by July 1st, or even before the end of the designated sixty-day period, I shall be delighted to withdraw this notice of cancellation of my Participating Physician's agreement.

Very truly yours,
E. TREMAIN BRADLEY, M.D.

Long before the advent of Connecticut Medical Service, Inc., most physicians observed the "Service Benefits" principle and, on a purely individual basis, adjusted their usual fee downward to accommodate the patient of modest means. I feel sure most of us will continue to observe this worthy principle, whether our patients have some form of insurance or not. As things stand now, however, I cannot continue an agreement binding me to a plan in which I no longer have a representative voice of my own choosing—the Connecticut State Medical Society; and I urge my colleagues throughout the State to take a long hard look at all the potentially undesirable consequences to their patients, to themselves, and even to CMS, that their continued contractual participation in CMS, as now being operated, is likely to engender.

Thank you.

E. TREMAIN BRADLEY, M.D.

Norwalk, Conn.

To the Editor

I enjoyed reading your editorials in the March issue of CONNECTICUT MEDICINE very much and would appreciate it if you would send me reprints of these editorials. I would cut it out of the Journal except that I give my Journal regularly to Good Samaritan Hospital for their library.

Incidentally as you may remember I used to practice in Connecticut, and am still a member of the Hartford County Medical Society, and get the Journal regularly which I enjoy very much and feel that you do a marvelous job and congratulate you for it!

Sincerely,

M. A. CRISPIN, M.D.

West Palm Beach, Florida

To the Editor:

This is a fan letter from a constant reader. I have been intending for some years to write you of my admiration for your editorship of CONNECTICUT MEDICINE and particularly for the pithy essays with which you ornament its pages. The April issue, with its succession of brilliant and timely reviews helped to remind me that my homage is long overdue.

As a medical school graduate of 1938, now completely at sea in the currents and controversies of modern medical science, I believe that a characteristic we must seek in prospective medical students is an abiding passion which drives them to remain abreast of the pertinent literature, or else we must imbue them with this desire during their medical school years. Otherwise, we run the risk of superannuating ourselves in about ten years, and the period of grace may grow shorter as the development of medicine further accelerates. Certainly, under your enlightened editorial leadership, the Connecticut physician is enabled to retain his acquaintance with the great issues of current medicine.

With best wishes,

PAUL E. KAUNITZ, M.D.

Westport, Conn.

To the Editor:

Dr. Louis Nahum discussed a broad specialty field with his usual fine insight in his recent editorial on, "Progress in Vascular Surgery."

I would like to state, however, that while Dr. DeBakey is rightly honored for his contributions, and plastic vascular prostheses are proving to be excellent for aortic aneurysm replacement, and are *sometimes* the best replacement for the aorta and its branches above the inguinal *ligament*, they are *not* the treatment of choice for arteriosclerotic occlusive disease of the arteries of the legs.

It has been my experience, and that of an increasing number of other vascular surgeons that the use of endarterectomy (of a more radical type than the earlier procedure bearing the same name) and autogenous veins used for bypass and/or onlay reconstruction has enabled a very high limb salvage even in limbs with distal gangrene and a seemingly hopeless prognosis. Dr. Robert Linton of Boston deserves great credit for his pioneering work in the development of these techniques.

They have the disadvantage of requiring considerably more operative time, but the advantages of autogenous tissue reconstruction are so great, that only under exceptional circumstances should a plastic prosthesis be employed in the leg.

Donald B. Alderman, m.d.

New Haven, Conn.

To the Editor:

The advisory committee to the Surgeon General of the Public Health Service, in it's extensive survey of the problem of smoking and health, has emphasized the apparent relationship that exists between smoking and an increased incidence of certain diseases particularly lung cancer. The fact that the use of tobacco requires a generation or more for the development of these diseases makes it most difficult to establish a clear cut cause and effect relationship. Animal experimentation cannot duplicate the circumstances under which cancer of the lung develops. It will require the examination of both smokers and non-smokers in similar environmental situations over a generation or more before proof can be more emphatically established.

Meanwhile, there appears to be a significant relationship between the use of tobacco in the form of cigarettes and the development of these disease entities. This should cause us grave concern in so far as assumption of the habit in the young is concerned. Once this habit is established, there is well known difficulty in becoming free from it. Therefore, the most important single attack on the problem of cigarette smoking is to prevent assumption of the habit in the young.

In the Danbury, Connecticut area under the auspices of the American Cancer Society students in the 7th and 8th grades and in the high school years are told in detail the findings of the Federal Advisory Committee hoping that those who have not assumed the habit will not do so.

We are urging those who are already habituated not to encourage others to follow suit. Parents, teachers and doctors must help in this matter even though they may be victims of the habit themselves.

Henry N. Blansfield, m.d.

Danbury, Conn.

Special Notices

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

September 17, 18 and 19, 1964

The Annual Fall Conference of the New England Society of Anesthesiologists will be held on September 17, 18 and 19 at the Lake Tarleton Club, Pike, New Hampshire. The guest faculty will include: Drs. Kenneth Keown, Joseph F. Artusio, Jr., William Dornette, Max S. Sadove and John Krantz.

CHEST PHYSICIANS PLAN MEXICO CONGRESS

October 11-15, 1964

"Physicians from more than 50 countries will present papers and discuss the recent advances in cardiovascular and pulmonary diseases at the VIII International Congress on Diseases of the Chest to be held in Mexico City, October 11-15, 1964.

Doctor Donato G. Alarcon, Dean of the Medical School at the University of Mexico and Professor of Thoracic Diseases is the President of the Congress and Doctor Ignacio Chavez, President of the University of Mexico and Professor of Cardiovascular Diseases is the Vice-Chairman of the Congress.

The Honorable Adolfo Lopez Mateos, President of the Republic of Mexico will officially open the Congress on Sunday, October 11th.

All physicians are invited to attend this important Congress. For further information and registration blanks write to the American College of Chest Physicians, 112 East Chestnut Street, Chicago, Illinois 60611."

COURSE IN POSTGRADUATE GASTROENTEROLOGY

October 22, 23, 24, 1964

The annual course in Postgraduate Gastroenterology of the American College of Gastroenterology will be given at The Roosevelt in New York City, 22, 23, 24 October 1964.

This year the Moderators for the Course will again be Dr. I. Snapper, Director of Medical Education, Brookdale Hospital Center, Brooklyn, N.Y. and Dr. John L. Madden, Clinical Professor of Surgery, New York Medical College and Director of Surgery, St. Clare's Hospital, New York, N. Y.

The faculty for the Course will be drawn from the Medical Schools in and around New York. The subject matter to be covered, from the medical as well as the surgical viewpoint, will be essentially, the diagnosis and treatment of gastrointestinal diseases and comprehensive discussions of diseases of the esophagus, stomach, pancreas, spleen, liver and gallbladder, colon and rectum. A clinical session will be held at The Mt. Sinai Hospital in addition to the several individual papers to be presented.

For further information and enrollment, write to the American College of Gastroenterology, 33 West 60th Street, New York, N. Y. 10023.

WOMAN'S AUXILIARY

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Report of The President Of The Women's Auxiliary To The House Of Delegates Of The Connecticut State Medical Society.

April 28, 1964

"1963 ℞—Serve and Communicate" has been the theme for the activities of the Woman's Auxiliary to the Connecticut State Medical Society this past year.

Having served on the County and State level in various offices, it has been my pleasure to have met doctors' wives with outstanding abilities. As State President I realize the potentialities of our Auxiliary members.

Our main purpose is to communicate with doctors' wives who can serve their physician husbands, the community and the Connecticut State Medical Society.

Our first project of the year was an Auxiliary Workshop with the SAC Program as a basis. It was divided into three parts. A—To operate efficiently, B—Program, C—Community Service. Members of the Board explained the various facets of the program, followed by a ten minute discussion period with a moderator. This Workshop was most rewarding and informative to the incoming Board of Directors.

Legislation has taken precedence this year. Urgent requests have come from the National Auxiliary and the President of the American Medical Association to be aware that this is the time to let your Congressmen and Senators know that the King-Anderson type of legislation is neither wanted nor needed. The County Auxiliaries started immediately on a writing campaign. The films, "Operation Hometown" and "The Gift of Health" have been shown in the counties and at the state board meetings.

There was no meeting of the State Legislature during this past year. However, there was a meeting of the State Health Council on fluoridation. Ten auxiliary members attended the hearing, signed the register and one spoke in favor of the bill.

A "Political Symposium" was held in January 1964 under the auspices of COMPAC. A panel discussion on the "Connecticut Political and Legislative Picture" was extremely informative and about 200 doctors and their wives attended.

It is with regret that our membership does not total what it did last year. We welcome new members and hope that they will be active as their dues do help the Auxiliary carry on its work in legislation, education and AMA-ERF. It is my belief that the hospital auxiliaries tend to lower our membership, which is only 1187 this year.

All county AMA-ERF chairmen and auxiliary members have cooperated in raising funds for our medical schools and the AMA Loan Guarantee Program. The outstanding fund raising event was "Theatre Night" sponsored by the New London Auxiliary when "Rebecca" was presented in Norwich. New London County also held their annual May dinner dance; Windham County their annual St. Patrick's day luncheon and bridge and Litchfield County a Valentine Dinner Dance. Fairfield County sold fruit cakes and New York World's Fair tickets; New Haven County had cake sales; Hartford County had a special committee studying the value of AMA-ERF and doubled their contribution from funds raised by their Ways and Means Committee; and Middlesex County made individual contributions. All counties used memorial and appreciation cards, sold playing cards and AMA-ERF note paper.

As a report for Community Service and Rural Health members of the Woman's Auxiliary cooperated with the Connecticut State Medical Society Rural Health Committee in the presentation of health, educational exhibits at nine county fairs throughout the state. The main purpose of the exhibits was to continue the program of encouraging residents to seek the council of their physicians about immunization against polio and other preventable diseases, mainly tetanus. Timely pamphlets were distributed. A survey of Homemaker Service Programs in Connecticut proved that volunteer work throughout the counties has been varied. Activities have included continuous uninterrupted delivery of meals-on-wheels, a service of the Hartford Health Department's Home Care Program. Volunteers also helped with eye screening at pre-school and glaucoma clinics, services of the Connecticut Society for the Prevention of Blindness. Also, they investigated the needs of senior citizens, visited hospitals and worked at mental institutions. Help was given with the preparation of Easter Seal envelopes, cooperation with local health departments in the administration of oral polio vaccine and assistance at speech and hearing clinics. In addition to the above mentioned activities the Cancer Society's film, "Is Smoking Worth It," was used in the schools of Windham County. Five thousand three hundred and fifty students and 170 adults were reached by the educational movie.

The *Connecticut Quarterly* has been published four times during this Auxiliary year and pertinent material has been submitted to CONNECTICUT MEDICINE for inclusion on the Auxiliary page each month. The Auxiliary appreciates the opportunity for space in CONNECTICUT MEDICINE through the courtesy of Dr. Louis H. Nahum and the Connecticut State Medical Society.

The health careers chairman and her co-chairman have been very active this past year. Connecticut has reached the "Cross Roads" in the health careers program. It is time to expand the horizon and obtain the assistance of other participating agencies which are members of the National Health Council. Mrs. Allen and Mrs. Chace attended a State Health Careers Committee meeting in New Haven in November. Mrs. Allen conducted the Connecticut Hospital Auxiliary Workshop in November. She also attended the first "Eastern Regional Conference on Health Careers" in New Jersey in December. The program to interest high school students in health careers is being carried on in several counties. A different approach in Fairfield County is pointing the way to a new consideration of the vital role hospitals can and should play in recruitment for health careers. Statistically speaking, in all probability, we will equal by the end of the 63-64 school year the good record of last year. Health occupations are now a "must" in the nation's working force. Mr. Burch mailed to various county newspapers copies of the following: Connecticut Health Careers Guidebook, Health Career Card, New Careers in the Health Sciences published by the National Health Council 1961, and Medical Careers published by the AMA.

Medical textbooks and magazines collected by International Health Activities chairmen have been brought to the Workshop of the Darien Book Aid Plan, Inc. This organization ships books and magazines to more than 60 countries throughout the world through the U.S. Information Agency to the U.S. Information Service Centers. Six tons have been shipped this past year. There is no government connection except as a depot for receiving material overseas. The material is usually sent "for Presentation to" certain medical schools, hospitals, clinics, etc., which have made requests although many sent are distributed as to need.

The Suicide Prevention Program inaugurated by the A.M.A. has been stressed by the National Mental Health Chairman. Most counties preferred to remain faithful to their previous commitments rather than inaugurate this project. Hartford County did, however, show the film "The Cry For Help" to its Auxiliary members and all county mental health chairmen. This was followed by a discussion period. Counties contribute hours of volunteer services to mental hospitals, hold picnics and parties for patients and coffee hours for closed ward patients. This is indicative of what is being done throughout Connecticut in the field of mental health, and certainly makes clear the dedication and interest that exists in the state in an area that very much needs all the help it can get.

Our representative to the Connecticut Advisory School Health Council, Mrs. Dewey Katz, reports that this Council is studying suggested means of improving health plans in the Connecticut School System. It is felt that the subject of Health Education has not yet attained the position it deserved in importance in the curriculum in every school, for the benefit of school children as well as adults who need more health education. Mrs. Katz was commended as well as the Auxiliary in being instrumental in the election of a representative from the Connecticut Society for the Prevention of Blindness to the Connecticut Advisory School Health Council.

All committees have functioned smoothly—finance, hospitality and publicity. We are honored this year to have Mrs. Morton Arnold as a Director of the Woman's Auxiliary to the AMA. Again, it is our good fortune to have Mrs. F. Erwin Tracy on the National Auxiliary By-Laws Committee, and Mrs. Norman Gardner as National Program Chairman.

I have presided at five board meetings, the Workshop, the semi-annual meeting and will preside at the annual meeting on April 29th. The president-elect and I have attended two conventions of the New York Auxiliary and the National Fall Conferences in Chicago. I represented the Auxiliary as presidential delegate to the AMA convention in Atlantic City in June 1963. I also attended the State Meetings of Rhode Island and Massachusetts as well as county meetings. The AMA-ERF chairman and I represented the Auxiliary at the Eastern Regional Workshop in New York in September. I was present at the Connecticut Health League meeting, the National Foundation Tour of the Birth Defects Special Treatment Center at the Grace-New Haven Community Hospital and the Steering Committee of the Connecticut Service Council, WNHC Stations.

Six of the seven organized counties in Connecticut gave scholarship aid of $6,700 to further education in medicine, nursing and health careers. Hartford County was outstanding with its grant of $3,600 to ten deserving medical students.

The AMA-ERF program has not quite reached the goal of last year. Four counties are in excess of the $5 per capita quota. Two counties lead with $8 per member and the other counties with $5 and $6. Most of this money will be used for the Loan Guarantee Fund. The highlight of the annual meeting April 29th will be the awarding of three certificates of achievement to the counties having been most successful in raising funds.

It has been a privilege to have served as President this past year. I appreciate having had a knowledgable executive board, diligent committee chairmen, and the enthusiastic support of each member. At this time I should like to thank Dr. William R. Richards and the staff of the Connecticut State Medical Society, also Dr. Morris P. Pitock and our able advisors Dr. Orvan W. Hess, Dr. Denis S. O'Connor and Dr. James R. Cullen for their support to the Woman's Auxiliary to the Connecticut State Medical Society.

MRS. FRITZ MEYER

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the following new books in their full page advertisement appearing elsewhere in this issue:

CHILD—THE LIVER AND PORTAL HYPERTENSION—New! The first of a series of monographs on selected major problems in clinical surgery. Covers all aspects of the subject.

1963-1964 MAYO CLINIC VOLUMES—New! The convenient way to keep up with newest developments from the Mayo Clinic. Both Medicine and Surgery are covered.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Advances In Metabolic Disorders. Edited by Rachmiel Levine and Rolf Luft, Volume 1, Academic Press, New York and London, 1964. 327 pp. $12.00.

The Immunologically Competent Cell. Ciba Foundation Study Group No. 16. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P. and Julie Knight, B.A. Little Brown and Company, Boston, 1963. 104 pp. with 18 illustrations.

Disorders of Language. Ciba Foundation Symposium. Edited by A. V. S. De Reuck, M.Sc., D.I.C., A.R.C.S. and Maeve O'Connor, B.A. Little Brown and Company, Boston, Massachusetts 1964. 345 pp. With 35 illustrations $11.00.

The Lung And Its Disorders In The Newborn Infant. Mary Ellen Avery, A.B., M.D. Volume I in the series Major Problems in Clinical Pediatrics. Alexander J. Schaefer Consulting Editor W. B. Saunders Company Philadelphia and London 1964. 224 pp. illustrated $7.50.

Communicable and Infectious Diseases. Diagnosis, Prevention Treatment, Fifth Edition. Franklin H. Top and Collaborators with 133 figures and 15 color plates. The C. V. Mosby Co. Saint Louis 902 pp. $21.00

Activities of Surgical Consultants. Volume II, Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army Office of the Surgeon General Department of the Army, Washington, D.C., 1964. 1100 pp. 365 ill. $8.50.

Fundamentals of Otolaryngology. A Textbook of Ear, Nose and Throat Diseases. Lawrence R. Boies, M.A., M.D. Jerome A. Hilger, M.D., M.S. Robert E. Priest, M.D., M.S. Fourth edition. W. B. Saunders Co. Philadelphia and London 1964. 553 pp. $8.50.

New And Nonofficial Drugs. J. B. Lippincott Co. Philadelphia and Montreal 1964 863 pp.

Modern Treatment. Volume I, Number I January Treatment of Renal Disease, Edited by E. Lovell Becker, M.D., Treatment of Thyroid Disease, Edited by Edward A. Carr, Jr., M.D. Hoeber New York, New York. A new bimonthly series. By subscription only: 6 books a year. 1200 pp. per year $16.00 per year.

ERRATUM: *On the April contents page, Mr. R. Rosen's degree status was incorrectly given as Ph.D. rather than M.Sc.*

OBITUARIES

Richard C. Buckley, M.D.

1907 – 1964

The Hartford area was deeply saddened on March 18, 1964, upon hearing the news of the sudden death of Dr. Richard C. Buckley at his home. Dr. Buckley was born March 1, 1897, in Brooklyn, New York, son of the late Mr. and Mrs. David Buckley.

He was graduated from Trinity College in 1919 and Yale Medical School in 1924. He remained at Yale after graduation in the department of pathology. He interned at Peter Bent Brigham Hospital in Boston and studied for several years under the late Dr. Harvey Cushing, world famous Neurosurgeon. In 1930 he was appointed to the staff of St. Francis Hospital and began private practice specializing in neurosurgery. He was truly a pioneer in this field in this area and became widely known throughout the State for the excellence of his work. He was chief of neurosurgery at St. Francis Hospital for many years and held appointments as a consultant in neurosurgery at the Newington Home for Crippled Children and the McCook Memorial Hospital in Hartford.

Dr. Buckley was a diplomate of the American Board of Neurosurgery and a Fellow of the American College of Surgeons. In 1955 Dr. Buckley was honored by receiving the Alumni Citation from Trinity College, an honor bestowed upon graduates who have achieved excellence in their field.

Dr. Buckley exemplified the life of a true dedicated physician. He was a tireless worker and whereas many men have side hobbies of one nature or another, Dr. Buckley's hobby was neurosurgery. A profound student, he continued his great interest in his work literally to the time of his death. He is survived by his wife Eileen, four children, Mrs. James Newell of Valley Forge, Pa., Richard C. Jr., Suzanne and Dianne all of West Hartford and six grandchildren, and one brother William E. Buckley of Huntington, Long Island.

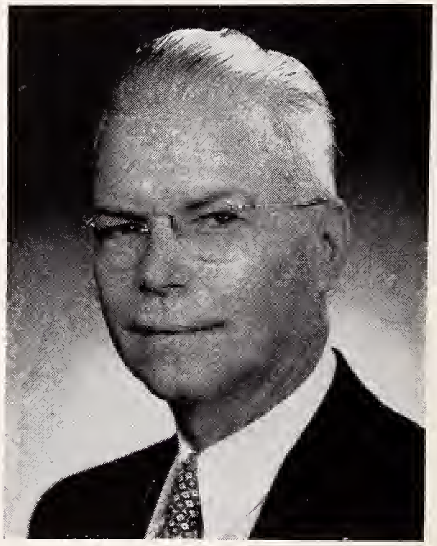
St. Francis Hospital and his many colleagues will long feel the loss of this distinguished physician and we would like to offer our deepest sympathy to his good family in the hour of their bereavement.

George C. Finley, m.d.

Frank T. Oberg, M.D.

1889 – 1964

Frank Thornwald Oberg, DeLand, Florida was born in Worcester, Massachusetts on August 26, 1889 and died on March 18, 1964. He was a graduate of Clark University and received his medical degree from Harvard Medical School in 1916.



After serving a two-year internship in the Worcester City Hospital Dr. Oberg started in general practice in Marquette, Kansas and two years later moved to Belgrade, Montana.

In 1926 Dr. Oberg came to Hartford. Here he was in private practice until June 7, 1943 when he went to the General Electric Company—Bridgeport, Connecticut – as head of their Industrial Health Department. In 1954, having arrived at retirement age 65, he returned to Hartford and resumed general practice. In 1958 he was compelled to retire because of ill health and permanent disability. He subsequently took up residence in DeLand, Florida where he died.

He was a member of the American Academy of Occupational Medicine, the Hartford Medical Society and a First-Lieutenant in the Army Medical Corps during World War I.

Throughout his varied medical career he was a diligent student and highly respected practitioner of medicine.

He is survived by his wife, Esther M. Oberg.

ARTHUR B. LANDRY, SR., M.D.

Joseph A. Fiorito, M.D.
1910 – 1964

Dr. Joseph A. Fiorito died suddenly at the Grace-New Haven Community Hospital on April 16, 1964, ending too soon a career already distinguished and promising even greater distinction.

He was born in Ripabottoni, Italy, on March 14, 1910, and came to the United States in his early childhood. He received his arts degree from Oberlin College in 1933 and his M.D. from Washington University, St. Louis, Mo., in 1937.

He trained in Surgery, Gynecology and Obstetrics in the New Haven Hospital, the Grasslands Hospital, Valhalla, N.Y., and the Royal Victoria Hospital in Montreal, P.Q. He completed his residency in Obstetrics and Gynecology at the New Haven Hospital in 1942 and practised those specialties in New Haven until the day of his death.

He served the Yale University School of Medicine as Associate Clinical Professor of Obstetrics and Gynecology and was appointed Chief of the Community Division of the Department of Obstetrics and Gynecology of the Grace-New Haven Community Hospital in 1952. The latter responsibility became the focal point of his professional life. A man of exacting standards, satisfied only by perfection, yet gifted with understanding and humor, he was conspicuously successful as "Chief" during the difficult times of merger of the staffs of the Grace Hospital and New Haven Hospital. He set a pattern for the job that leaves scant room for improvement. He has left indelible his stamp on one of the country's finest Obs.-Gyn. services.

Never meant to be a passive bystander, Joe enjoyed his deep involvement in the affairs of the Yale New Haven Medical Center. Always conscious of the problems of house officers, he concerned himself with their affairs at all levels. He brought the finest talents of physician, teacher, and administrator to a difficult and important job. There was never doubt about his stand on controversial matters and his approach was direct and honest.

His selfless devotion to his family, his patients, and his profession makes keen our deep sense of loss. Others will take up his duties, but he will never be replaced in the hearts of his family, friends, patients, and associates.

ROBERT R. BERNEIKE, M.D.

Louis Loffredo, M.D.
1894 – 1964

Dr. Louis Loffredo died March 25th at the age of 69. He received his M.D. degree from the University of Pennsylvania Medical School in 1922.

Dr. Loffredo was an able surgeon and general practitioner. He was chief of the senior attending surgical staff at Middlesex Memorial Hospital from 1929 to 1937 after which he operated his own private hospital, the Crescent Street Hospital. He was a Fellow of the American College of Surgeons, and held membership in the Central Medical Society, Middlesex County Medical Association, Connecticut State Medical Society, and the American Medical Association.

Besides conducting a busy practice, Dr. Loffredo found time to take an active part in civic affairs. He was one of several physicians and public-spirited citizens who worked to obtain a full time health department for the City of Middletown in 1937 and served as a charter member of the Board of Health since then. Dr. Loffredo was a member of the Middletown Board of Education for the past ten years and served on the Middletown Redevelopment Commission for several years.

Those who knew Dr. Louis Loffredo remember him as a rugged individual whose foremost interest in life was his love for the practice of medicine to which he devoted himself to his last days.

Mario L. Palmieri, m.d.

In Memoriam

Davis, George B.—Norwalk; University of Vermont Medical School, 1924. Dr. Davis was health director for Norwolk from 1948 until his death. He was past president of the Connecticut Public Health Association. He was a member of the American Medical Association, the Connecticut State Medical Society, the Fairfield County Medical Association, the American Public Health Association, and the American School Health Association. Dr. Davis died April 27, at the age of 69.

Kilbourn, Joseph B. — Hartford; College of Physicians and Surgeons, Baltimore, 1911. Dr. Kilbourn was the organizer and chief surgeon of the Imperial Royal Austrian Ambulance Train at the start of World War I. Being one of the first doctors to perform battlefield surgery during World War I, Dr. Kilbourn was decorated by the Austrian Emperor and Prussian government for surgical work on the Russian, Italian, Bulgarian and Carpathian fronts. During World War II, Dr. Kilbourn was a member of the National Draft Board and president of the Friends of Austria, Inc., an organization devoted to helping refugees and the restoration of freedom in Austria. Pope Pius XII cited Dr. Kilbourn for his refugee work in 1948. Dr. Kilbourn served on the staffs of Hartford and McCook hospitals and the Hartford Dispensary. He was an attending physician at Cedarcrest Sanatorium in Newington. Dr. Kilbourn was a member of the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. He died May 10, at the age of 75.

Zonn, Seymour I.—Waterbury; Tufts Medical School, 1917. Dr. Zonn was a practicing physician in Waterbury for 17 years. During World War I, he served in the United States Navy Medical Corps as a lieutenant (j.g.). Dr. Zonn was the founder, president, and administrator of the Middlebury Convalescent Hospital, in Middlebury. He was a member of the International College of Surgeons, the American Geriatrics Society, the American Academy of General Practice, the Phlebology Society of America, the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, and the Waterbury Medical Society. He was a Fellow of the American College of Angiology. Dr. Zonn died April 6, at the age of 71.

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

General surgeon—board eligible, 34, married, university trained—5 year residency: military service completed; desires association with surgeon (s) or group preferably in or close to urban area in Connecticut.

PLACEMENT OPPORTUNITIES

WANTED—Part time psychiatrist in hospital in Hartford County.

WANTED—Pediatrician in New Haven County.

WANTED—Part time pediatrician in New Haven County.

WANTED—Radiologist (diagnostic) in 300 bed general medical and surgical hospital in Hartford County.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN ST., NEW HAVEN.

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Vitamin B_1 (Thiamine Mononitrate)	10 mg.
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AMA-AAHPER Endorses Exercise As Aid To Physical Fitness

Exercise as an important part of overall physical fitness was strongly endorsed by a joint committee of the American Medical Association and the American Association for Health, Physical Education, and Recreation.

The committee, in a statement published in the current *AMA Journal,* said reasonable exercise was good for anyone "organically sound" and gave the reasons why, including the probability of enjoying a longer life.

"Belief in the healthfulness of regular, suitable exercise, previously based on tradition and logic, is constantly being bolstered by evidence from research," the statement said.

"As far as can be determined at the present time, the study of the life histories of those who maintain a relatively higher degree of fitness through the nature of their work or other activities seems to indicate that they suffer less degenerative disease and probably live longer than those who follow a sedentary life.

"The benefits of physical activity are more clearly observable in their relation to certain organic diseases. Regular exercise is now considered to help retard the onset or further progress of diabetes, for example, and man's most common threat to health —atherosclerosis [a form of hardening of the arteries].

"There is no longer any doubt that the level of physical activity does play a major role in weight control. The high mortality rate associated with being overweight suggests that obesity contributes to organic degeneration."

The possible effects of prolonged inactivity, the statement added, are obesity, wasting away of muscles, heart and circulatory inefficiency, joint stiffness, and impairment of energy-converting functions of the body.

In essence, the committee continued, the greatest contribtion of exercise to fitness is "improved organization of the body functions which support activity."

This improved physiological efficiency is reflected in increased endurance, strength, and agility, it said, adding:

"The oftener the normal heart and circulatory system are required to move blood to active regions of the body, the more efficient they become. This is accomplished chiefly by improved muscular tone of the heart, an increase in its output of blood per minute, and an increase in the number of active capillaries in the lungs.

"Protracted exercise improves the work of the lungs by increasing their ability to expand more fully, take in more air, and utilize a greater proportion of the oxygen in the inspired air.

"Games and sports involving extended running, vigorous swimming and dancing, and other sorts of forceful effort serve this purpose. Activities of this type involving leg muscles also help to maintain good circulation against gravity through a 'milking or 'squeezing' action of the muscles on the veins. This benefit cannot be achieved by any other means."

Prolonged inactivity, on the other hand, results in a decline in circulatory and lung efficiency, the committee pointed out.

The committee stressed that a program of exercise should be started at an early age and be continued throughout life with certain adjustments from time to time as life advances and needs, interests, and capabilities change.

"The nature and severity of the exercise should be graded according to age, individual reaction to activity, and the state of the person's fitness. After age 30, more frequent medical evaluation of the individual's capacity for exercise is imperative.

"There is a considerable range of individual variation in need and capacity for exercise. A physically active person may need little, if any, additional exercise to maintain fitness, whereas an inactive, relaxed person must add exercise to prevent becoming less fit.

"The amount of vigorous exercise that is desirable each day is largely an individual matter. Recommendations range from 30 minutes to an hour daily as a minimum.

"Advanced age, in itself, is not a contraindication to exercise, but is actually an indication for it. Precluding accidents, a healthy person of any age will do himself no permanent harm by suitable physical activity."

The potential for muscular strength usually reaches a maximum in early adulthood and most persons in their 30's and 40'es experience a gradual decline of strength, endurance, and agility, the committee explained. The heart and circulatory system also tend to exhibit a lessening of functional capacity for exercise and resilience in recovery after exercise.

"The extent and rapidity of this decline is partly dependent on exercise habits in adult life," according to the statement.

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Also available with ¼ gr. codeine as SOMA® COMPOUND WITH CODEINE: carisoprodol 200 mg., acetophenetidin 160 mg., caffeine 32 mg., codeine phosphate 16 mg. (Warning: may be habit forming).

WALLACE LABORATORIES/ *Cranbury, N.J.*

Side effects: Although there has been no evidence of tolerance, withdrawal symptoms or excessive self-medication, 'Soma' Compound and 'Soma' Compound with Codeine, like other central nervous system depressants, should be used with caution in addiction-prone individuals. While codeine addiction is relatively rare and easily broken, the same precautions must be observed as for any other opium alkaloid. Nausea, vomiting, constipation and miosis are possible codeine side effects. Should symptoms of hypersensitivity occur, discontinue medication.

Contraindications: None reported.

Complete product information available in the product package, and to physicians upon request.

Dosage: Usual dosage is 1 or 2 tablets 4 times daily.

Supplied: 'Soma' Compound is available in orange, scored tablets; bottles of 50. 'Soma' Compound with Codeine (narcotic order form required) is available in white, lozenge-shaped tablets; bottles of 50.

CSO-1054

Usually, it was pointed out, the untrained individual stops exercising long before his physiological limits are reached. However, exercise carried to the state of exhaustion may do harm, particularly to the unconditioned individual, the committee warned.

"If breathlessness and pounding of the heart are still noticeable 10 minutes after exercise, if marked weakness or fatigue persists after a two-hour period, if a broken night's sleep is attributable to exercise, or if there is a sense of definite and undue fatigue the following day, then the exercise has been too severe or too prolonged for that person in his present stage of training and phyiscal strength."

Comparing physical capacities between men and women, the committee said on the average there are measurable differences in heart capacity, muscular strength, and skeletal proportions.

"However, the range of physical capacities in individuals of each sex is much greater than the avereage differences between sexes," the committee added.

Commenting on isometric exercises, to which some attribute gain in strength in shorter periods of effort than needed for traditional isotonic exercises, the committee said:

"In isometrics, a vigorous muscular contraction is sustained for a brief period without producing movement; in isotonics, muscular contraction produces a range of movement of body parts. Since isometric exercises have no beneficial effect on range of motion, and present difficulties in motivation, they should be considered as only part of an exercise regimen. Neither isometric nor isotonic exercises improve circulatory endurance unless involved in a total activity that taxes the cardiovascular and pulmonary system."

Committee members are Warren R. Guild, M.D., Boston, Frederic T. Jung, M.D., Evanson, Ill., and Allan J. Ryan, M.D., Meriden, Conn., AMA, and Henry J. Montoye, Ph.D., Ann Arbor, Mich., Laurence E. Morehouse, Ph.D., Los Angeles, and M. Gladys Scott, Ph.D., Iowa City, Iowa, AAHPER, with Fred V. Hein, Ph.D., director of AMA's Department of Community Health Education, Chicago, serving as editor.

Rheumatic Fever Program Change Announced

The Rheumatic Fever Secondary Prevention Program sponsored by the Connecticut Heart Association, Connecticut Pharmaceutical Association and the Drug Wholesalers of Connecticut, has been changed with respect to the reapplication procedure. The reapplication form will now be a part of the prescription book in the form of a business reply post card (green). It will now become the responsibility of the attending physician to complete and mail the reapplication form upon issuing to his patient, the 4th (last) prescription stub from the current book. Upon receipt of the reapplication card, the Connecticut Heart Association will mail a new ℞ book (one year's supply) to the physician immediately, or as soon as one year has passed since the last ℞ book was issued.

This change in procedure is another effort to facilitate continuity of daily prophylaxis to prevent recurrent attacks of rheumatic fever for those enrolled on the program. The coded prescription and prescription stubs will remain an integral link in the procedural chain to help with follow-up reporting to physicians on those patients delinquent in taking their penicillin daily, as well as for other statistical reports.

The change will be effective with new ℞ books issued after May 1, 1964 and the conversion should be completed in approximately one year.

Lung Cancer Mortality

A Public Health Service study of 683 women has shown a lung cancer death rate of 101.4 per 100,000 population, for female smokers. Earlier data for male smokers have established a lung cancer death rate of 392.8.

The present study also reveals that for female non-smokers, the lung cancer death rate is 9.4, compared to 12.5 for male non-smokers. This difference by sex is in line with that for most causes of death.

These and other findings were obtained in a survey of lung cancer mortality as related to residence and smoking histories conducted by Public Health Service scientists, and reported as Part II in April issue of the *Journal of the National Cancer Institute.* Part I of the study, on white males, was published in the April 1962 issue of the same journal.

In the latest investigations, William M. Haenszel of the National Cancer Institute and his colleague, Karl E. Taeuber, now of the University of California, collected residence and smoking histories from relatives of a 10 percent sample of white females who died of lung cancer in the United States during 1958-59.

In general, findings for females agree with the earlier ones for males. For example, the more women smoke, the greater their chance of developing lung cancer; and the risk is greatest for heavy smokers who move frequently and for the foreign-born settling in large cities. However, place of residence does not seem to play as important a role in determining lung cancer risk for women as for men smokers. There is no evidence that in females the effects of urban residence and excessive smoking enhance one another. In men, the combined effect of excessive smoking and urban residence is greater than expected.

Future investigations are planned in which detailed information will be collected on such aspects of cigarette smoking as brand preference and age at which the habit was established. Mr. Haenszel and Mr. Taeuber believe that such information will make it possible to measure more precisely the degree of smoking exposure for each person studied.

Postgraduate Education For GPs

Recently in England, a report from the "Research Project on Prescribing," University of Liverpool, which deals with "the extent to which a doctor interprets and correlates his scientific information when he is applying it to the needs of individual patients," has been published. . . . The report is concluded by these observations: "Medical training, the pharmaceutical industry, the *British National Formulary* and consultants were each employed to provide over 20 per cent of the information which general practitioners need for treating their patients. . . . Information from the drug industry was used for 60 per cent of the diseases." . . . Our observations over the years would lead us to believe that what was found to be true in England, is probably true in the United States. It points up beyond doubt the large contribution which the pharmaceutical manufacturers are making to the post-graduate education of family physicians in this country. In this effort the industry should be aided in every way by investigators, and government, so that correct clinical therapeutic information may be quickly made available to those who treat the bulk of disease, the family physicians of the United States.—Perrin H. Long, M.D., in *Medical Times,* Dec. 1963.

AMA Motion Picture Catalog Now Available

The most complete catalog ever compiled of medical and surgical motion pictures has been published by the American Medical Association

The new book, "Medical And Surgical Motion Pictures," lists over 3,000 available motion pictures dealing with every phase of the healing arts. Up-to-the-minute listings were made possible through computer processing.

The AMA "Medical And Surgical Motion Pictures" catalog will be an invaluable tool in the training of students, nurses, and graduate physicians. This catalog is aimed at the potential user of films of a professional nature and includes films for personnel in ancillary fields of medicine.

The film listings are divided in three general categories: basic sciences, clinical medicine and surgery, and para-medical sciences. It is then subdivided into some 600 specialty subjects. The films are listed alphabetically under each specialty.

Included with the listing is a brief summary, running time, black and white or color, silent, optical or magnetic sound, year of release, language versions other than English, names of the authors and producers, and the name and the address of the primary rental source. Films have been chosen which are readily available in the United States. In many cases a critical evaluation of the motion picture is included with its listing.

Present plans call for the catalog to be updated periodically.

The "Medical And Surgical Motion Pictures" catalog is available at the cost price of $5.00 to addresses in the U. S., U. S. Possessions, and Canada; $5.50 to other foreign addresses. Write to the American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

ECG By Radiotelemetry Clarifies Diagnosis

Electrocardiograms continuously recorded by radiotelemetry have been used to clarify the reasons for recurring fainting spells and have prevented unnecessary surgery in three patients, three Duke University physicians reported recently.

Four patients with heart block who suffered blackouts were referred to Duke University Medical Center for implantation of electrical pacemakers to correct the problem, according to Drs. Gordon H. Ira, Walter L. Floyd and Edward S. Orgain, Durham, N. C.

However, by continuously monitoring the patients' heart activity it was learned that the fainting episodes were not related to heart block in three cases and pacemaker implantation was not the appropriate treatment, the authors wrote in the current *Journal of the American Medical Association.*

Continuous monitoring of a 60-year-old woman for nine days revealed that her fainting spells were not associated with changes in heart rhythm. Other studies then uncovered the presence of a tumor in the upper right chamber of the heart. The tumor was removed by surgery and she has had no further fainting spells. Although the patient still has complete heart block, a condition in which the upper and lower heart chambers beat independently, she returned to her normal activities.

By the same process, the fainting spells of a 33-year-old woman were found to be caused by hyperventilation, abnormal deep breathing marked by confusion, dizziness, numbness, and muscular cramps. She was treated without surgery.

Continuous monitoring also helped to find the underlying causes of fainting in a 61 year-old woman who was treated successfully with drugs.

In the fourth patient, continuous monitoring confirmed that heart block was associated with fainting and a pacemaker was successfully implanted.

The radiotelemetry system consists of a small, specially designed battery-powered FM transmitter capable of transmitting the electrocardiographic impulses for 72 hours which is placed on the patient, leaving him completely free to perform any sort of activity without hindrance, the authors explained. The signal is sent to a modified FM receiver where it is taped and can be studied on an oscilloscope and other machines.

Prolonged, uninterrupted recordings of this type were not possible until the miniaturization of electronic equipment allowed the monitored patient free movement.

Widely Used Chemical Causes Bizarre Effects

Thiram, a widely used chemical compound, is a rare cause of allergy but can cause a bizarre reaction in conjunction with the ingestion of alcohol.

Thiram and its derivatives are components of numerous fungicides, insecticides, seed disinfectants, larvacides, germicidal soaps, lotions, ointments, rubber goods, and disulfiram, a drug used to treat alcoholism, according to an article by Dr. Walter B. Shelley, Philadelphia, in the current *Journal of the American Medical Association.*

The alcohol reaction can cause flushing and an itching skin eruption shortly after alcohol is taken by persons who ingest disulfiram or are exposed externally to thiram, Dr. Shelley said.

Danish physicians discovered in 1948 that thiram and its derivatives sensitize an individual to alcohol. The drug, disulfiram, later came into use as a means of dissuading alcoholics from drinking.

That external exposure to thiram also produces alcohol sensitization was first reported by M. J. Villiaumey in 1954. He described a man using thiram ointment and powder who developed temporary flushing, swelling and burning of the face and neck when he drank wine or other alcoholic beverages.

Dr. Shelley also cited the case of a woman who experienced flushing of her face every time she drank a cocktail and then took a bath with soap containing thiram.

The alcohol phenomenon is a pharmacological reaction, he explained. More rare is the allergic reaction which occurs when a person previously sensitized to thiram later comes into contact with the chemical, he said.

The case of a 51-year-old man who developed a progressively more severe skin inflammation from July, 1959, until August, 1963, was reported by Dr. Shelley. Investigation revealed that he had regularly used a soap which at one time contained thiram and later had come into contact with the chemical through a thiram turf fungicide used to spray a golf course on which he played.

Thiram has been known to be a skin sensitizer since the early 1920's when it was first detected as the cause of a skin disease in certain workers in the rubber industry, according to the article. Thiram is used as a catalyst in the vulcanization of rubber.

In the 1930's it was discovered that thiram was a powerful fungicide, Dr. Shelley said, and it is now being used to treat the soil, the seeds, the plants, and even the products of fruits, vegetables, nuts, and mushrooms.

"Although thiram and its congeners are not common sensitizers, it is evident that an appreciable number of farmers and gardeners today must suffer from disclosed or undisclosed hypersensitivity to them," he added.

Special Book Issue Published By JAMA

Recent medical books in six general areas are reviewed in the current special book issue of the *Journal of the American Medical Association.*

Books on cardiology are reviewed by Drs. G. E. Burch and N. P. DePasquale, New Orleans; on psychiatry by Dr. R. R. Grinker Sr., Chicago; on endocrinology by Dr. T. F. Frawley, St. Louis; on gastroenterology by Dr. J. B. Kirsner, Chicago; on medical genetics by Dr. V. A. McKusick, Baltimore, and on pulmonary disease by Drs. R. S. Mitchell and G. F. Filley, Denver.

"On the medical scene the book forms an indispensable basis for medical education, both undergraduate and graduate," according to a JAMA editorial.

"In this special issue we try to bring medical books into relation with the wider world of letters, as well as to discuss some less known aspects of medical communication."

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Under the pressure of modern living, with its "small continued anxieties of life,"[6] functional disturbances of secretion, tone and motility of the gastrointestinal tract are extremely common.[6,8] For the relief of symptoms associated with such disturbances—through rest for the patient, rest for the colon[3]—the drugs of greatest value have proved to be the antispasmodics and the sedatives.[3,6,7]

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CONTRAINDICATIONS: DONNATAL is contraindicated in acute glaucoma, advanced hepatic or renal disease, and known or suspected idiosyncrasy to any of its components.

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BOOK REVIEWS

SYNOPSIS OF PEDIATRICS by James G. Hughes, M.D. The C. V. Mosby Co., St. Louis, Missouri. 1963, 1031 pp. $9.85.

Reviewed by: LOUIS H. NAHUM

There is room for a book in pediatrics that is not as lengthy and detailed as a text, nor so brief that basic fundamentals are inadequately covered. In this synopsis accurate information is readily available. There is present in it a strong orientation towards explanation of the fundamental mechanisms of disease and it successfully bridges the gap between basic science and clinical features. This allows a full appreciation of disease processes and permits logical application of therapy.

The challenge of medical writing today is to combine brevity and clarity with the right amount of comprehensiveness. To over condense, and oversimplify are double dangers which Professor Hughes and his twenty colleagues have deftly avoided. A new method of medical illustration evolved by the author, is used here for the first time. It consists of organ arrow and label overlays superimposed upon the picture of a child. These are ingenious and excellent for making teaching slides or illustrations.

There are twenty-five chapters and an appendix of seventy-nine pages. There are a few typographical errors. The chapter on the psychological development of the child is clear and lucid, but does not base its description on a clear analysis of ego psychology, and the known factors in its development. This, however, does not seriously detract from its usefulness.

This synopsis will help the physician and the specialist to keep abreast of the rapid strides that are being made in clinical pediatrics and should be on every doctor's desk, and in the hands of every medical student and interne.

THE PEDIATRIC PATIENT 1963, David Baird Coursin, M.D., Consulting Editor, Sarah R. Gustafson, Ph.D., Co-ordinating Editor. Published by Roche Laboratories, Nutley, New Jersey, 1963. 183 pp. $4.95.

Reviewed by: VICTOR L. SZANTON

Here we have a refreshing summary of what's new for the physician interested in pediatrics. Emphasis is placed where it belongs. The importance of heredity and metabolic disorders in relationship to DNA and RNA is given priority. The recent advances both theoretical and factual are delineated using sickle cell anemia as a prime example. Whereas the practitioner is given no solution to clinical problems in this field, it does give him a vantage point from which to comprehend and await further developements in this new break through which begins to unravel the underplay of DNA, RNA, enzymes and genetic material. The magnitude of the problem is clearly stated in pointing out that more than a hundred thousand kinds of proteins have been identified in the human body alone. One cell may produce from one thousand to two thousand proteins. How the protein characteristic of each tissue and organ, the thousands of specific enzymes, hormones and antibodies, all proteins, are passed on to the successive generations of organisms with faithful reproduction is the engrossing question.

It is obvious that this field of research brings forth more questions now than it does answers. Studies have been done in regard to DNA and RNA relationships in the structure of proteins such as insulin, and the capsular substance of bacteria among many others. That such research is now in work is in itself encouraging. The infinite variety of possible DNA, RNA enzyme combinations may at first be just as awe inspiring as the field of bacteriology was in its early days but which ultimately has been brought down to the level of practical use and therapy.

There as another section devoted to the inborn errors of metabolism. This brings forth the high lights of the more frequent illnesses such as phenylketonuria, galactosemia, myasthenia gravis, mucoviscidosis and also cautions the reader that the list of inborn errors of metabolism now has increased to a list of over fifty.

The portion dealing with microbial therapy reviews the mechanism of action on bacteria in regard to cell capsule, membrane and cellular cytoplasm as well as the difference in activity of bacteriocidal and bacteriostatic drugs. The penicillins, the tetracyclines, neomycin, canmycin are discussed from this view point. There is an excellent review of the uses of sulfonamide in pediatric practice.

Lesser chapters deal with other pediatric areas as well as current attitudes and concepts to tonsillectomy and adenoidectomy.

This is a small volume that covers a great deal of ground. It will be a boon to those who feel swamped by the overwhelming tide of published papers. It will be a stimulus to those more courageous souls who still are in the swim for more knowledgeability.

THE LUNG AND ITS DISORDERS IN THE NEWBORN INFANT. Mary Ellen Avery, A.B., M.D. This is Volume I in the series "Major Problems in Clinical Pediatrics," Alexander J. Schaefer, Consulting Editor. W. B. Saunders Company, Philadelphia and London, 1964, 224 pp., illustrated, $7.50.

Reviewed by: LOUIS H. NAHUM

The author, Dr. Avery, is Assistant Professor of Pediatrics, Johns Hopkins University and Pediatrician in charge of "Newborn Nurseries," The Johns Hopkins Hospital.

The idea for this series arose with the Consulting Editor, Dr. Schaefer who felt there should be one volume in which old and new information widely scattered in numerous periodicals or too compactly compressed in a few pages of a standard text-book, should be brought together. There are individuals who have amassed much information on a particular subject who can in a monograph mark the point of farthest advance of knowledge in this decade. Dr. Avery has had a broad experience as physician, teacher and investigator. She is as intimately acquainted with a "cyanotic newborn infant in the nursery and with a newborn lamb attached to a variety of measuring instruments."

The book she has produced is remarkable. She has described and explored the lung of the newborn infant in its normal and then its many abnormal ones. Part I is devoted to the lung embryologic development, its anatomy, its vascular supply both pre- and post-natally and its physiology. She has correlated a vast material on fetal and neonatal mammalian lungs both in full-term human newborn infants and premature ones.

Part II presents in similar detail the clinical radiologic and laboratory manifestations of all the known disorders of the respiratory tract of newborn infants ranging from Channel atresia to pulmonary hemorrhage. Their abnormal physiology, pathologic alterations, pathogenesis and therapy receive careful attention. The author's management of the hyaline membrane syndrome towards which much of her own studies have been directed, is outstanding.

Together with the well recognized entities, she also describes some that may be new to many of us including the Wilson-Mikity syndrome and pulmonary lymphangiectasis. Her section on asphxia neonatorium and the one on resuscitation of the asphyxiated newborn comprise absolutely the last word as of 1964 on these highly important topics.

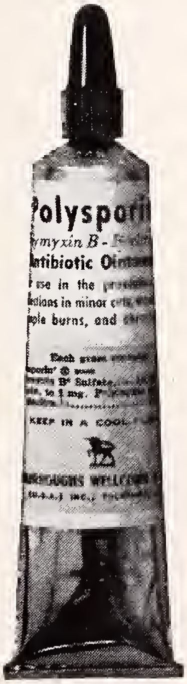
The volume contains many illustrative charts, diagrams, tables and X-ray photographs. Its bibliography includes the impressive number of nearly 600 references. If the successive volumes in this series turn out to be of equal exhaustiveness and usefulness, we are in store for an intellectual and scientific treat of great usefulness to the pediatric specialty. As usual Saunders has done an outstanding job in printing, type of paper, plate reproductions.

HOSPITALS AND CHILDREN*, *Edited by James Robertson. International Universities Press Inc., New York, 1963, 159 pp. $4.00.

Reviewed by: VICTOR L. SZANTON

Hospitalization, American style, for a preschooler is a caution for which we are all forewarned. Children in this age group are expected to be upset, concerned, anxious, worried, fearful, afraid, and deserted, and so they are!

We are told to reassure the child that he is not being deserted, that hospitalization is not a punishment, that the doctors and nurses that needle him are his friends, that such pain and discomfort as occurs will go away, that he will be coming home as soon as possible. Also, we tell him what is going to happen and why it is necessary. We are also told to leave him a favorite toy and a trinket or an every day article of "Mommy's." We are also apprised of what to expect in the "post hospitalization" period: sleeplessness, enuresis, thumbsucking, fussy eating and regression to earlier behavior patterns in general. The British feel differently about this matter. They feel the hospitalized child should be treated as a child—that the mother should be permitted to stay and sleep in the room with the hospitalized child as



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much as possible. This book is concerned with reactions of mothers of hospitalized children, with "rooming in" mothers versus traditional separation of children from parents. It deals with medical as well as surgical patients in this regard. The British have greater knowledge and experience with the matter of parentectomy—probably based on valid Blitzkrieg experiences of the past. Their updated handling of hospitalized children calls for careful consideration on this side of the ocean. Practical application of this idea would undoubtedly reduce psychic trauma to the hospitalized preschooler.

SYNOPSIS OF OBSTETRICS, Sixth Edition by Charles E. McLennan, M.D. The C. V. Mosby Co., St. Louis, Missouri, 1962, 464 pp. $6.75.

Reviewed by: LOUIS H. NAHUM

The first edition of this excellent synopsis was authored by the late Professor Jennings Crawford Litzenberg in 1940. It was then an illustrated expansion of a set of lecture notes that had been made available in mimeographed form to Minnesota students for many years. It reviewed in concise pithy statements the subject in a more or less outline form and was designed to, and certainly succeeded in, arousing the attention of the student.

The present author who is Professor of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto, California has prepared the last two editions as well as this one, and has rearranged almost the whole book. It now follows a more logical sequence and has merged much related subject matter that previously was widely scattered. For example, the various abnormal labor mechanisms have been combined into a single chapter and relocated beside other items pertaining to dystocia. Formerly six short chapters were devoted to coincidental complications of pregnancy. In this edition they have been combined in one chapter on medical and surgical disorders associated with gestation. Postpartum hemorrhage which formerly was linked with ante partum hemorrhage has now been linked with other accidents of the third stage of labor.

The book is new in the sense that considerable amounts of outmoded material has been deleted and many new sections have been added so that it can be considered as expressing the latest in obstetric belief and practice. Few pages have escaped revision of some sort. Many old illustrations have been replaced and new figures added so that it is a synopsis which will be of inestimable help to the student and an excellent guide to the teacher as to how to present this subject to his students.

THE FALLEN SKY. Medical Consequences of Thermonuclear War. Saul Aronow, Ph.D., Frank R. Ervin, M.D., and Victor W. Sidel, M.D., Eds. Hill and Wang, New York, 1963, pp. 134.

Reviewed by: REUBEN I. H. SOLWAY

In a quietly dramatic, thought-paralyzing article in the New England Journal of Medicine (266: 22: May 31, 1962) called "Human and Ecological Effects in Massachusetts of an Assumed Thermonuclear Attack on the United States" a group of physicians and physicists drew a picture of the detonation of a medium-size (20 megaton) Fusion Bomb at ground level in down town Boston.

The article and ancillary material have been collected into a book, "The Fallen Sky" designed to answer such questions as:

1. What are the dimensions and characteristics of thermonuclear war?
2. What is the physician's role in the post-attack period? How many physicians will survive? How many patients will each physician be called upon to attend? How effective can he hope to be, even under conditions of maximum preparedness?
3. Who will survive and how? Is civil defense an illusion? How about civilian shelters?

We all remember the enthusiasm that was generated just two years ago for the family-style shelter that could be built in the cellar for about $200, or the more elaborate shelter that could be installed, half-buried in your back yard. We pass these monstrosities on the roadside today: a cast-iron tank with a hooded chimney, or a box of corrugated tin with a double-blind door. Common-sense in those days told us that these gadgets were of only limited use; as we read this book, we can see that these containers would serve only as incinerators.

The blasts of Hiroshima and at Nagasaki were puny by modern standards. The postulated 20 megaton ground-blast would excavate a crater 300 feet deep and half a mile in diameter with an area of total destruction having a radius of four miles. Even at a distance of 15 miles, shock waves alone would kill or seriously injure 15 per cent of the population.

The Hiroshima blast carried little of the thermal range of the contemporary bomb. We had a preview of fire-storms during World War II when conventional bombs killed 300,000 people in Dresden in a single night, in Hamburg some 70,000 and in Tokyo some 200,000. Some days after the raid on Hamburg the heat remaining in the shelters was sufficient to cause them to burst into flames on being opened. Although the blast effect of the thermonuclear device increases only as the cube-root of the size of the bomb, the thermal effect increases as the square-root of the bomb size, and the resulting fire storm far outdistances the blast.

The fall-out in the Hiroshima blast was comparatively negligible; in the thermonuclear blast the fallout would be fatal to 50 per cent of the population within a tweny-mile radius, although a high wind may account for deaths 100 miles away.

The authors estimate that this one bomb would kill 2,000,000 people in metropolitan Boston by blast and heat alone. Beyond the blast area a considerable number would succumb to fallout.

Since the physician population tends to be concentrated in the metropolitan area, casualities will be proportionately higher among the medical men. As a result about 75 per cent of the physicians would be knocked out, leaving each survivor to care for 1,000 to 1,700 acutely injured persons. Not inconsiderable will be the persons surviving the attack who *believe* they have been injured. If all the stock-piled hospitals planned (not yet constructed) by the Federal Civil Defense Administration were to remain undamaged,

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and if the roads to them remained intact, and if personnel were available to man them, they would provide less than 1 per cent of the beds needed to care for the acutely injured. The stock piling of drugs and supplies would be similarly inadequate. The problems of moving equipment and surviving physicians into contaminated areas beggars the imagination.

The social and psychiatric considerations raised by a shelter program are viewed in humble credulity. The cartoon of the man standing shot-gun in hand at the doorway of his shelter is a synopsis of the ethical problem; more important is the response of his family and of his children to long-range confinement. Gerard Piel raises the question, "If fall-out shelters can secure a substantial number of survivals, what kind of world will they survive into?" He points out that such a war would decimate our population and destroy most of our industrial capacity. The logistics of recovery would be such that a large surviving population would fare poorly compared to a small group because of the lack of industrial capacity.

In the final chapter, Bentley Glass discusses "The Biology of Nuclear War." In addition to the consequneces of radiation upon the human organism, he calls attention to the widespread changes in terrestial flora. Since insects are resistant to high-energy radiation, they would be the dominant form of animal life and will quickly destroy all remaining vegetation.

"The Fallen Sky" is an important book. It cuts through much of the wishful thinking that motivates our current civil defense program. It calls for a re-evaluation of the basic conseqeunces of thermonuclear war to humanity in general, and of the responsibilities of physicians in particular.

MEDICAL DEPARTMENT U. S. ARMY—PREVENTIVE MEDICINE IN WORLD WAR II, VOLUME VI—COMMUNICABLE DISEASES. Colonel John Boyd Coates, Jr., M.C., U.S.A., Editor-in-Chief. Ebbe Curtis Hoff, Ph.D., M.D., Editor for Preventive Medicine. Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., 642 pp. $6.25.

Reviewed by: DENIS S. O'CONNOR

When the entire history of the Medical Department of the U.S. Army in World War II is written, I doubt if any volume will approach this volume in overall importance.

Devoted in its entirety to the problem of malaria in all its phases, and covering a large part of the globe, it is a source book identifying the various members of the mosquito family, their breeding grounds, their biting habits, their animal preferences—practically every aspect of information which one should know to meet the problem of their control. The geographic and climatic conditions which influenced the propagation of mosquitoes, the value of various chemicals in the destruction of the mosquito and their larvae, the preferential method of distributing the chemicals under varying conditions, the control of mosquito in housing, the personnel measures to avoid mosquito attacks, the suppression of the symptoms of the disease, the identification of the type of plasmodia and the treatment of the disease itself, all these are meticulously covered for each location where malaria was a problem and there was scarcely any area in which American troops were located that did not have the problem.

It is quite obvious that we did not anticipate the magnitude of this problem, if we recognized it at all, and for most of the duration of the war the problems were ahead rather than behind us. However, out of the studies which were necessary and which were essential to the proper handling of this disease has come the most comprehensive body of knowledge on this subject which can be found at the present time in one volume.

Any control had to start with a determination of the presence of the disease in the native population and the particular form, or forms, of the disease. The vectors—mosquitoes—had to be trapped, identified, and their habits studied, the area had to be surveyed to determine the conditions which favored the propagation of the mosquitoes and the most effective larvicides determined, as well as the most effective method of applying the larvicide for the area involved. Means of eliminating breeding places involved considerable engineering study and the application of much labor to drain larval locations.

Since no single measure could be depended upon to eliminate this military scourge, spraying of living quarters, body protection of persons necessarily exposed to mosquito attack by proper clothing and use of mosquito repellents were necessary. Probably the most necessary and difficult problem was to indoctrinate the men themselves in the importance of use of all measures, including the suppressive—atabrine.

In theatres of operation it was not possible to eliminate the mosquito ahead of time and suppression of symptoms of the disease became the first and most important measure.

Unfortunately, our ignorance of the military importance of this disease not only by our troops but by our officers and some of our doctors, resulted in a disdain for the disease and disregard for the use of the atabrine until the malaria had created a military crisis. Even then the imposition of stern measures and strict control was necessary to put into effect the measures necessary to meet the problem.

It would be impossible in a short review of this most valuable work to do justice to the vast amount of information contained within the covers of this book.

While anyone interested in malaria itself—the types of mosquitoes found throughout the world, the geographic and climatic conditions favoring their propagation, the public health aspects of this problem to say nothing of the means which have been developed to meet the various aspects of this problem—should have this source book in his library. It will be an irreparable loss to future military expeditions if from this store of information is not developed manuals for doctors, field officers and enlisted men which will enable them to more adequately meet this threat to military effectiveness in the future.

One can be sure that in many areas of the world where the disease was controlled for military reasons, it is even now the same problem it was before.

The world health organization could well consider action against conditions favoring malaria and in future military actions a public health organization to work with Army, Navy and Air Force might not be such a bad idea.

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MEDICAL QUACKERY: MAX CAPLAN, M. D., GUEST EDITOR

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RAMÓN Y CAJAL: NEUROANATOMIST (see page 491)

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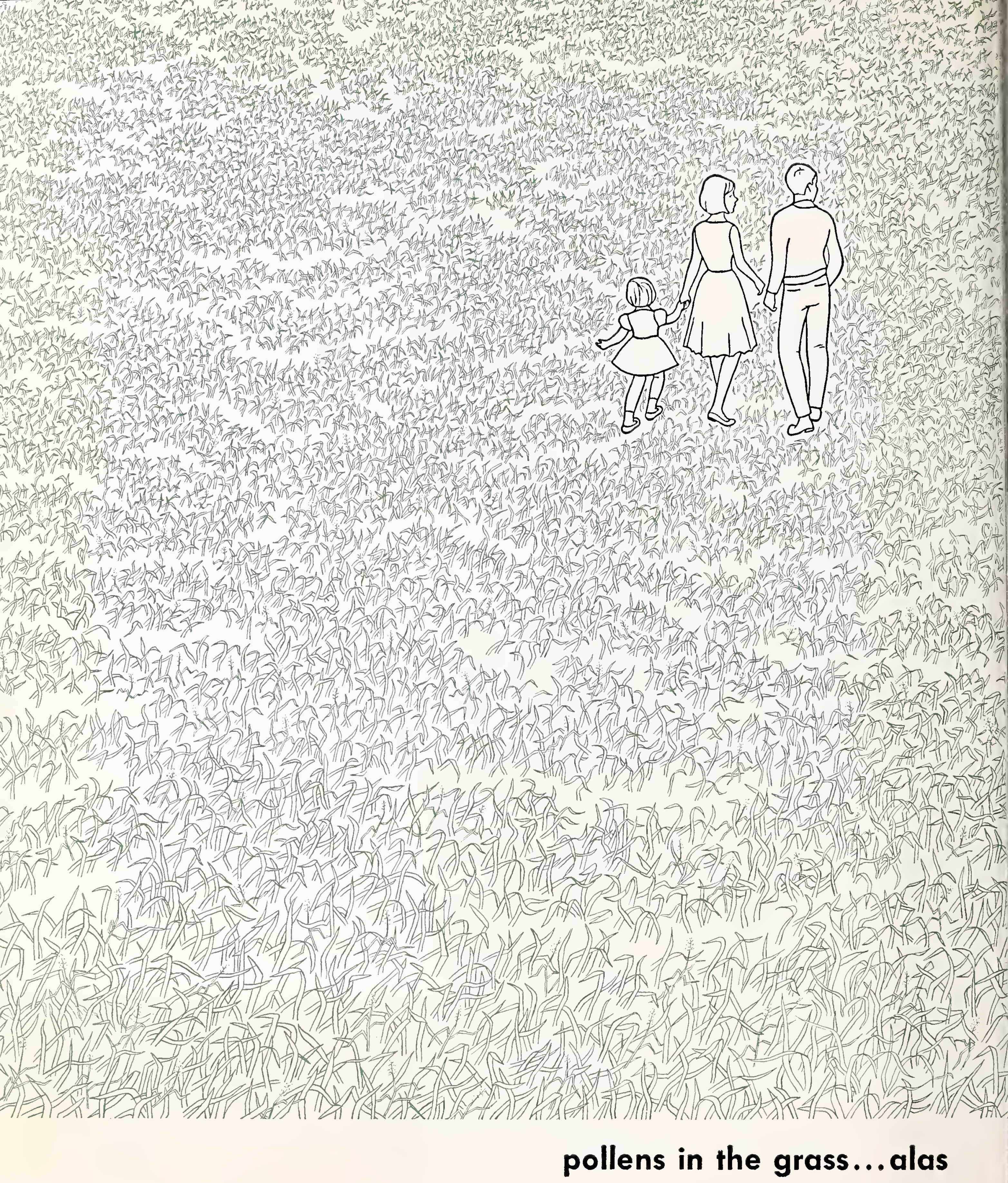

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editorials

Medical Quackery

Who are the people who are mostly involved with medical quacks? Are they those affected by superstition and magical thinking; those affected by fears of death or mental or physical incapacitation; those who have emotionally immature personalities; those who are looking for something for nothing; those who have been told that their doctors have no further medication which can help them? Can it be that some members of the public go to quacks because they do not think too highly of their doctors? Can it be that many people feel that their doctors are too busy, are not interested, don't explain, don't even know certain things? Do the people feel that the doctors are letting them down with their books such as: "Folk Medicine," "Calories Don't Count," and books which have been written by reputable doctors and members of their medical societies? Does the public feel that doctors do rigged research, advertise with weasel words, or use phrases taken out of context? Has the public lost faith in us because we still cannot give them a definite answer about the dangers of high cholesterol, the use of Enovid, or cancer cures such as Krebiozen?

Only answers to these questions can solve the two billion dollar medical quackery racket which involves unsuspecting victims not only of their money but their chance for cure, their hopes, and the considerable benefits of modern medicine. When education which starts in the grade schools and continues throughout the high school and college levels is directed toward teaching our public how to spot the medical quack, perhaps they will not be taken in by the doubtful uses of bottled sea water, royal jelly, female breast developers, male baldness cures, pimple cures, etc. They may learn to spot the impossible and the incredible and realize that any one medicine which can promise health, beauty, athletic ability, radiant living, the capacity to stay young, to say nothing of curing arthritis and rheumatism, cancer, and all forms of malnutrition, has not yet been developed and never will be.

The American Medical Association, the American Cancer Society, the American Heart Association, the Arthritis and Rheumatism Foundation, and the Better Business Bureau have all joined to help to expose a great many of these frauds. The Better Business Bureau itself since the First National Congress on Medical Quackery has published reports on the medical worthlessness of the advertising claims for do-it-yourself sulphur baths, baldness cures, sea water products, insomnia treatments, breast developers, laxative preparations alleged to have weight reducing qualities, depilatories, height increasers, and tobacco habit cures. It has warned against such things as house to house vitamin promotion, air purifiers, massage and exercise devices, skin tanning preparations, hearing aids, and Christmas perfume hoaxes.

Fake colleges and fake degrees are still very much in the news. For a few dollars one can obtain a spurious degree of Diplomat of Massotherapy, Philosopher of Metaphysics, Master of Character Analysis, or any one of 250 others, mostly by mail. One can still obtain the degree of Doctor of Chiropractic, Naturopathic, Medical Psychology, Philosopher, Divinity, Theology, Master of Herbalist, or Doctor of Botanic Medicine. All that is required is that a charge of $150 is paid for each degree, and more than 100 of the spurious degrees duplicate titles of degrees offered by legitimate institutions. There are innumerable individuals practicing law,

THE COVER

RAMÓN Y CAJAL: NEUROANATOMIST

BOYHOOD teachers were positive that no good would come from backward, headstrong Santiago Ramón y Cajal (1852-1934), but the country surgeon's son was destined to became Spain's leading medical scientist and a world-renowned neuroanatomist. His contributions to neurology and to pyschiatry began in a crowded laboratory in Barcelona. For forty years, Ramón y Cajal combined insatiable scientific curiosity, inventiveness that resulted in new stains for sections under his microscope, intensive observation, and inborn artistic ability, to reveal a wealth of new anatomical and functional facts about the nervous system, and about disorders affecting it. He received the Nobel Prize in medicine in 1906.

medicine, dentistry, engineering, ministry and other professions with only academic credits purchased through degree mills, and there are, today, in the United States hundreds of degree mills functioning. Only two of our States have adopted some corrective or preventive legislation against this insidious practice up to now, while ⅔ of our States have no law to prevent anyone from legally hanging out a shingle and calling himself a psychologist. This encourages psychoquackery to flourish since the public is confused as to what truly qualifies an individual to treat the human mind. They have still not yet learned that qualified professionals in this field are either psychiatrists, psychoanalysts, or clinical psychologists.

The medical quack is really a two-gun man who says "your money AND your life." He cannot be laughed out of business nor is any one agency big enough to do him any real harm. It will take the combined efforts of all of us as well as our Federal Government with its Food and Drug Administration, the Post Office Department, the Federal Trade Commission, the Department of Justice, and the Department of Health, Education and Welfare. The two great National Congresses on Medical Quackery which were held in Washington under these combined auspices have done a great deal to acquaint us with the problem and to direct us toward possible solutions. Additional State Conferences such as the one these papers are from, are extremely valuable in that they bring the problem down to our level and present it to many more doctors than the few delegates from here who attend the National Conferences. It may still be possible to stamp out the world's second oldest profession but it will take a Herculean effort from all of us.

Max Caplan, M.D.,
Guest Editor.

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1. From the First National Congress on Medical Quackery—October 6, 1961.
2. From the Second National Congress on Medical Quackery—October 25, 1963.

The First Recorded Murder Conviction Of A Medical Quack

Professor Curran in a recent publication[1] brings to the attention of our profession a very unusual kind of murder case which raises important questions not only with regard to medical quackery, trends towards a more vigorous enforcement against medical quacks, and also, what may be the obligations of an attending physician and pathologist to report neglect or refusal of medical care by a patient which may lead to premature death or even unnecessary disability.

It appears that a unique medico-legal section was established in the Los Angeles County District Attorney's office in 1963 under Chief Deputy District Attorney John W. Minor.[2] It is the first section of its kind ever established in a criminal prosecuting agency in the United States and the chief reason behind it was a medical quack murder case.

It appears that the Epping's daughter was in a hospital and the parents were informed that the child suffered from a rhabdomyosarcoma entirely confined to one eye. An operation was advised and if it had been performed at this time, it would have prolonged the child's life much beyond the time the child actually lived. However, before it could be performed, the parents happened to talk with some other parents at the hospital who told them that Dr. Phillips had cured their son of a brain tumor without surgery! The Eppings immediately called Dr. Phillips, described the situation and asked if he would help. He is alleged to have replied, "Yes, absolutely." Accordingly, the parents withdrew their daughter from the hospital and entrusted her to Dr. Phillips care.

He treated her for some three weeks and during this interval the tumor grew considerably. Dr. Phillips was discharged when the tumor had grown to the size of a tennis ball. The parents did not again seek medical care but turned to Christian Science, leaving the child to die about two months after Dr. Phillips was discharged.

Professor Curran proceeds to ask some searching questions. Is Phillips a murderer? Mr. Minor asserted in the case of People vs. Phillips,[3] that under the felony-murder rule, a defendant is guilty of murder if he kills a person while committing another felony, this even if he does not intend to kill. He is guilty of murder even if he merely hastens death, if even by only a few weeks. Minor contended that Phillips had defrauded the Eppings and this had, as one of its results, the premature death of their child. Minor contended that Phillips intervened just after the child's condition was diagnosed and at that time an operation might have saved the child's life or at least would have prolonged it beyond the time she actually died.

Dr. Phillips was convicted of second degree murder on the felony-murder rule and also under the rule of "proximate cause." He was sentenced to five years to life. It is currently under appeal and obviously some very serious legal questions are involved that will take months to settle. No matter what its outcome, it reveals a trend towards a more vigorous enforcement program against medical quacks. Professor Curran points to two national conferences in the past few years devoted to this subject and that the Phillips case is part of a strong legal effort currently under way to protect children

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from a variety of harm. Some of these programs will obviously require reporting to authorities such instances that come to the attention of physicians and pathologists.

There are battered-child reporting laws. But what are our obligations to report actions such as those of Dr. Phillips, when they come to the attention of a pathologist only at the time of the child's death? And what obligation is imposed on an attending physician or pathologist to report neglect or refusal of medical care by a parent? The Phillips case certainly gives reasons to raise these issues and perhaps many others.

L.H.N.

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Science Tools:
5. The Infra-Red Spectrograph

Science and technology are the hallmarks of our society and differentiate it from all that has gone before in human history. The notion that thinking is man's highest activity while technical skill is relegated to inferior individuals has vanished with the scientific revolution. Technical innovations are arising with such profusion that it is almost impossible to keep up with them. Not a week goes by, but a new instrument or device is offered the medical profession which aids in diagnosis and therapy. They occur so quickly that it is almost impossible for society to absorb them. The laboratory chief has become the indispensable link between advancing science and the practicing physician. The *Journal* hopes from time to time to bring to the attention of our readers important advances in technology which are and should be made available to the physician to sharpen his diagnostic skill and perfect his therapy.

An instrument which could rapidly and accurately identify toxic substances in a patient's breath, blood, and clothing could often be of paramount importance. For example, a patient is brought to the emergency room that is thought to have diabetic coma and would ordinarily be treated with large doses of insulin, but a quick analysis of his blood revealed he was poisoned by isopropanol.[1] Or take another patient brought into the emergency room suspected of having carbon monoxide poisoning. A quick examination of the blood revealed that the patient was actually poisoned by carbon tetrachloride and ethylene dichloride. The instrument capable of making these differential diagnoses rapidly is the infra-red spectrograph.

Infra-red analysis of the patient's expired air requires no sample preparation and may be used to identify virtually any organic compound which is slightly volatile at room temperatures. These include carbon monoxide and other heterotonic gases; carbon tetrachloride and trichlorethylene; various alcohols such as methanol, ethanol and isopropanol; ketones, such as acetone, methyl-ethyl ketones; ethers, esters, aldehydes, paraldehyde dioxane and others.

Infra-red analysis of blood and other body fluids following extraction with an appropriate solvent may be used to analyze all the above compounds except the very light gases. In addition, the extraction method may be used to detect less volatile materials such as drugs soluble in certain organic solvents, like barbituates, dicoumarol, metabolites and degradation products such as acetone, benzoic acid, phenols.

There are two other uses of infra-red analyses such as identification of medications and toxins in solid or liquid forms and identification of pesticides in contaminated clothing following solvent extraction. Why is it that infra-red spectrographic methods are ideally suited to toxicological analysis. The answer is that each organic compound possesses a specific infra-red absorption spectrum or "fingerprint." This spectrum arises from absorption of infra-red energy at certain frequencies which depend upon the particular atoms and forces within the molecule. Erley and Stewart[1] point out that this is probably the characteristic physical property of an organic compound and that in most cases the infra-red spectrum of a compound may be used to identify and quantitatively to analyze it. The samples may be analyzed as solids, liquids or gases and the depth of the absorption band is proportional to the amount of the material present. This makes it possible to perform quantitative analyses on mixtures. Sensitivity to many compounds can be extended to the parts per million. The method is rapid since analysis of an unknown requires about thirty minutes.

To date the chemical industry has had the greatest experience with these infra-red methods and breath analysis of workers exposed to solvent vapors has become a vital emergency room procedure. Their ability to identify quantitatively various compounds following air exposure to a mixture of vapors has proved beyond a doubt that breath analysis is an indispensable diagnostic test.

The inherent speed and simplicity as well as specificity of the infra-red method makes it ideally suited to emergency room toxicologic problems. If it is good for industry why is it not good for the public in the emergency room evaluation of a patient suspected to have been overcome by a toxic substance? It is a highly versatile method and eminently applicable to many types of medical and toxicological problems. It is claimed that the initial cost of setting up an infra-red laboratory is high and training of an analyst in its use expensive, so that the method will probably be limited to emergency room application of these methods to poison centers or to the larger medical centers with infrared facilities.

At the University of Michigan Medical School Center, infra-red analytical methods have proved of value in at least three realms: identification of toxic solvents in the patient's breath in the post exposure period; identification of drugs and other organic compounds, and determination of blood and breath actetone concentrations in diabetes. But even in a university center, the full diagnostic prowess of the tool has not been utilized, for the service has not yet been made available to the house staff covering the emergency room nor have all the physicians been instructed in the potential uses of spectrographic analysis.

If money is the only deterrent to the widespread use of this powerful tool, perhaps one less spaceshot would release enough funds for this valuable instrument to be introduced and made functional in every emergency room of the country.

L.H.N.

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Mutual Medical-Dental Problems

In health the homostatic mechanisms are so effective that a powerful stressful stimulus is dampened out so that it may be registered by only a slight response or none at all. On the other hand in patients suffering from cardiovascular disease, a slight stressful stimulus may be followed by an overwhelming response. They are delicately balanced and need protection against both emotional and physical trauma. In such patients dental treatment must be modified to avoid adverse effects. To reduce the amount of dental care necessary it is obviously desirable that patients with cardiovascular disease should have periodic dental examinations, so that required treatment can be instituted early, thereby avoiding much dental procedures.

The cardiovascular patient has special problems which will require special precautions, when dental procedures become necessary.[1, 3] He may be taking hypotensive drugs. He may have angina pectoris. He may have rheumatic heart disease and require prophylaxis to prevent bacterial endocarditis. He may need to be protected against extensive dental procedures. His vascular system may be sensitized to vasoconstrictor drugs and require special precautions against intra-arterial injections. He may be taking anti-coagulant drugs, whose sudden cessation might lead to thrombosis. For all these reasons the management of dental problems will require mutual understanding and co-operation between the physician and dentist. The dentist should discuss the medical aspects with the physician, and the physician on his part should know the extent and type of dental procedures and drugs to be used so that a treatment program can be mutually agreed upon.

The drugs that require special precautions when dental treatment is necessary are the diuretics and antihypertensive drugs. These may predispose to orthostatic hypotension and patients may faint when changed from a relatively prone to a sitting or standing position. In addition reserpine, guanethidine and ganglionic blocking agents may potentiate the response to epinephrin in the local anesthetic. For this reason the anesthetic should be injected slowly, the plunger drawn back before injecting to avoid intravascular injection. Intravascular injection of local anesthetcs is particularly dangerous to patients with cardiovascular disease. Intra-arterial injections provoke distant anesthesia and blanching of the immediate area, while intravenous injections may cause central nervous system stimulation or depression, hypertensive crises or dangerous degrees of myocardial ischemia. Instruments commonly used by dentists do not allow for preliminary aspiration. However, aspirating cartridge syringes are available which provide safety for the patients, fewer anesthetic failures and fewer anesthetic reactions. General anesthesia is particularly hazardous in patients with angina pectoris or coronary artery insufficiency and should be avoided at all costs, short of a hospital environment.[4]

Saliva inhibiting drugs such as atropine and methantheline should not be administered to patients with cardiovascular disease since the dosage of either drug commonly used in dental procedures often produce tachycardia which can be a burden on a sick heart.

Angina pectoris can be precipitated by apprehension. If an attack occurs during dental treatment all procedures must be interrupted and nitroglycerin taken according to instructions from the patient's physician. It is well for the dentist to have such pills available in his office should the patient

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
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have failed to bring them along. To allay apprehension and prevent or minimize blood pressure rises during the waiting room period as well as in the dental chair it is desirable that the patient should receive preanesthetic sedation with short acting barbiturates. Pentobarbital or secobarbital in a dosage of 30-100 mg. is satisfactory for most adults although the dosage must be on an individual basis and the drug carefully administered. The premedication should be given in the waiting room at least 45 minutes before dental procedures. If the patient has a history of not tolerating barbiturates well, a tranquillizing drug may be used instead. As a precautionary measure all patients who receive premedication should have someone accompanying them to drive them home.

Dental procedures are not of the same magnitude and no hard and fast rule can be established for the amount of dental work that should be done at any one time. All depends on the amount of trauma involved and the patient's ability to withstand trauma. If extractions are needed, one or two teeth removed at one time will reduce the trauma, chances of bacteremia and other complications. The ability to withstand dental procedures is greatly compromised when a patient is recovering from a coronary heart attack and it is best if at all possible to avoid dental procelures for at least a period of three months after the attack.

Prophylactic antibiotic therapy is indicated in all patients with rheumatic heart disease or congenital heart disease who require extraction of teeth or other oral surgical procedures or manipulation of periodontal tissue. The majority of patients can be protected by appropriate anti-microbial agents. The drug of choice is penicillin and the treatment schedule is outlined by the Committee on Prevention of rheumatic heart disease and bacterial endocarditis of the American Heart Association.[5] It should be pointed out that no antibiotic dosage regime is completely effective in preventing bacteremia and subacute bacterial endocarditis so that the dentist must be very careful to avoid all possible trauma.

Many physicians use anticoagulant drugs as a long term therapy in patients with coronary artery disease and in some form of threatened strokes. It is therefore important to know that if such treatment is continued at full doses profound bleeding may occur. On the other hand sudden withdrawal of anti-coagulant drugs especially if Vitamin K preparations are administered are followed by a "rebound" increase in clotting and actually promote thrombosis or embolism.[2] It is therefore important when extractions or periodental surgery is contemplated in a patient receiving coumarin drugs, that the physician in consultation with the dentist, should gradually reduce the dosage of anticoagulant drugs to maintain a prothrombin time of 1½ times the control level. Dental surgical procedures can then be performed without undue bleeding if the operative site is sufficiently limited to permit the effective use of local procedures for hemostasis, including absorbable hemostatic agents, sutures, and prolonged pressure applied to a gauze dressing over the wound.

Dentists are well aware that any emergency may occur in a dental office in patients with known cardiovascular disease or as a manifestation of such disease. Dentists should suspect cardiac emergencies when the patient experiences chest pain, persistent breathlessness, or prolonged fainting or unconsciousness. When confronted with such a problem a physician should immediately be summoned. Oxygen should be administered to patients with chest pain who do not respond to nitroglycerin. Epinephrin should be avoided. If unconsciousness occurs both physician and dentist should be familiar with the signs of cardiac arrest and be prepared to institute closed chest cardiopulmonary resuscitation until the patient is brought to a hospital.

L.H.N.

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The Crisis In General Practice

There is a plaintive cry for the "doctor" of yesterday in many lay publications. The fact is, he does not exist and if he did there would be no place for him in today's medicine. Years ago before the age of specialization it was not unusual for an untrained general practitioner giving the anesthetic and another acting as scrub assistant and a third, a product of a one year rotating internship entering an abdomen. We have gone far beyond this primitive phase. Now the administration and control of surgery, anesthesia, internal medicine and the other specialties are the zealously guarded privileges and responsibilities of the members of these groups. As these groups enlarge, the general practitioner has declined even though our population has increased. The decline in general practice is a fact, what is its etiology.[1, 2] Obviously the graduate of today has other thoughts about entering general practice than he had a generation ago. Even now with each succeeding 5 year period after graduation an increasing number of physicians leave general practice for a specialty.

Many reasons have been offered for this phenomenon. Military service rewards the specialist and so interns and residents strive to make themselves proficient in a specialty. Then of course there are some who fail to achieve success in general practice and seek for greener fields in some specialty. There are also those who become disenchanted with some aspects of general practice, (long hours, night calls, desire to live in a city, lack of status in the hospital, limited intellectual stimulus, lack of change of pace and poor health). Even super-success can be a cause in some instances since it leads to financial independence thereby allowing the physician to leave the arduous life of general practice.

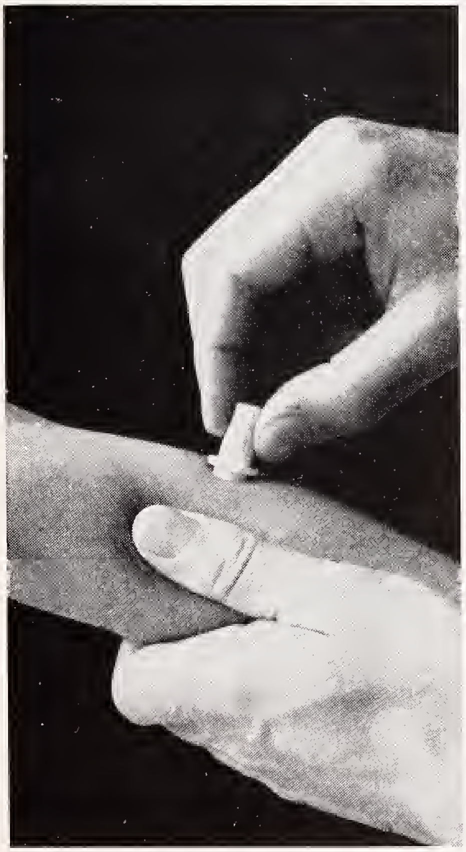
There are also other reasons for disenchantment with general practice.[3, 4, 5] As medical coverage of the population increases by medical insurance, it usually pays the physician only when his patient is hospitalized and the general practitioner is not often on a hospital staff or if he is, his pay is not as much for the same service as that of a specialist. Another reason is the general practitioner's involvement in furnishing continuous care often for chronic illnesses that are not curable. In today's world the public and doctor alike often expect a cure or a miracle drug or operation for every ill with the result that patients inevitably drift toward the specialist who often can do more for the patient than his family doctor. The family physician often finds himself without proper preparation for managing this type of chronic problem, since he is trained by specialists who are accustomed to provide episodic care of illness. As a result he may become frustrated and decide to become a specialist, a career in which he expects to see fewer of his failures.

To these specific causes for the decline in proportion of physicians in general practice must be added another compelling one—our failure to demonstrate decisively what it is that the family physician can do better than the specialist. For it must be admitted that the medical student does not contemplate with equanimity any activity in which he will be second best. Already the medical student, house officer and practitioner all believe that the family physician i really only second best to the specialist. If this turns out to be correct the general practitioner faces extinction except in some isolated areas that cannot support specialists. Perhaps this is too pessimistic a picture. However, until University departments of family medicine, practitioners and organized medicine address themselves to this question and carry out carefully designed experiments in different types of medical care to establish what it is that the specially trained family physician can and cannot do best, a decline in general or family practice must continue.

The family doctor will have a rebirth when his role is clearly defined and when he is specifically trained for this job, and the superiority of his care is demonstrated over the forms of medical care by specialists.[6] In addition his personal satisfaction will also have to be increased hopefully through collaboration with University departments of family medicine.[4, 6] Haggerty[2] suggests that the University department might have a small group of family physicians to whom first class comprehensive medicine could be given and collaborative research with the practitioner in the area undertaken. Such research will reveal problems and add to the personal satisfaction and the status of the practitioner. Such researches might even stimulate students' interest in the field of family practice. As of today, however, the drift away from general practice is continuing relentlessly. The number of graduates going into specialty training is increasing by leaps and bounds, approaching 85 per cent.[3] It is not unlikely that one day practically all physicians will be going into specialty training and no general practitioners will be available.

At this moment internists and pediatricians do fill in some way the vacuum left by the vanishing general practitioner but they cannot have the wide range of interests in or concern for the family that was the special province of the general practitioner. Neither in internal medicine nor pediatrics is there any evidence that training for these specialties is anything but in the direction of the consultant with command for larger fees and not too great concern for the family. If the internist and pediatrician be come interested in family practice it is by pure chance and counter to the training they receive.

We are not going to make family physicians by changing the medical curriculum.[4] Hospitals emphasize laboratory skills, deal with complicated illness and are becoming increasingly depersonalized and lack any emphasis or focus on the family. To believe that the curriculum modification will direct students to family practice is to ignore the realities



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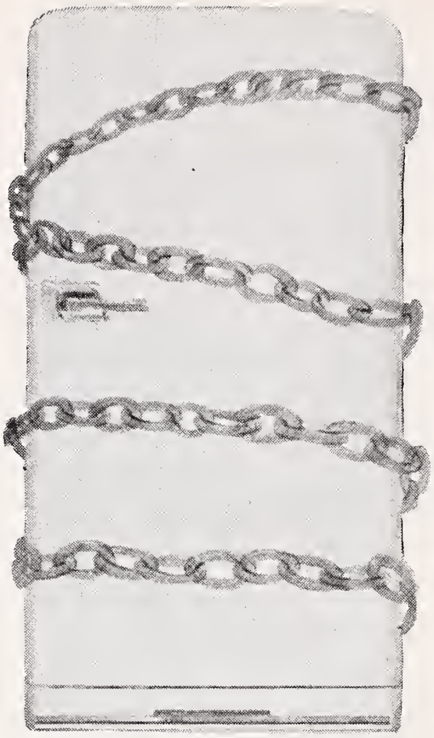

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of medical practice. No sensible student wants to spend 3-4 years becoming a general practitioner, to work harder, earn less, and be barred from hospitals. In the medical school the student learns to accept physiological and biochemical bases of practice not the sociological ones the family physician is up against. In short if we wish to increase the number of family physicians we must create situations in which one of the specialties will be family practice. Such a specialist must know internal medicine, psychiatry and the sociological field of the family.[4] He must be aware not only of physical illness, but also of interactions of family members, community and socioeconomic and environmental factors affecting the health of family and members. This would of course be one way to resolve the current dilemma to make family practice a clear specialty field comprising a body of special knowledge and training. It would then become an area of study and research and service as distinct as that of any other specialty. For there is already developing today specialized knowledge about the interaction of illness and families as complex and as worthy of investigation as any other field of the natural sciences. Our difficulty has been to introduce sociological science into the already crowded curriculum on the same footing with the natural and biologial sciences.[4]

At present the student can see the vanishing general practitioner but no rising family specialist. There is no model to hold up before our students. It is not easy to move students in the direction of a wholly new enterprise which has a very doubtful base. Existing specialists have considerable status, practice in hospitals, charge higher fees and have other prerequisites of professional prestige. Specialism is a necessary component of modern medical practice. It cannot be dislodged or undermined. If family practice is to be preserved it must become a specialty on a par with all the others. It is not likely that the student will be drawn into a field in which no attributes of specialism obtains.

If the practice of medicine were reorganized into a group practice in which all income was pooled and distributed according to a formula equal pay for equal work then the specialist in general practice would be assured of similar working conditions and equal status with the surgeon, obstetrician or internist. But most practice in this country is not group practice and most doctors do not provide for pooled income and redistribution on an equal work equal pay schedule. Why should a physician undertake added training for family practice and not acquire the professional and economic attributes of other specialists?

This then is the crisis in general practice. It is rapidly losing ground. Students are going into specialties. Unless family practice can be made into a specialty as worthy as any of the others it will in time become extinct. No amount of lectures, preceptorships, professorships, or departments of general practice can avail against the powerful tide of specialism and the associated professional and economic benefits.

L.H.N.

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"Hazards" And "Episodes" In Hospital Practice

> *"First of all be sure you do not harm—*
> *Primum non Nocere."*

In the last eight years three important papers[1, 2, 3] have called attention to harmful effects of drugs and procedures especially those that have been encountered in a University Hospital. This is not surprising when we consider the multitude of new relatively untried diagnostic and therapeutic procedures which form an integral part of the practice of medicine. Diagnostic methods which were formerly single are growing complex and becoming increasingly formidible. Our best practice sanctions the use of injections of organic substances for visualization of almost every artery and every organ. Our best practice cannot avoid reactions from digitalis, antibiotics, allergic reactions from a wide variety of new drugs. There are now hundreds of separate drugs which are known to cause allergic reactions.

Our best practice cannot avoid the dangers of multiple procedures. We know that the dangers inherent in diagnostic and therapeutic procedures came not so much from the use of individual tests or drugs as from the multiplication of these measures now commonly used in so-called diagnostic surveys. Patients in a diagnostic clinic or in the ward of a modern hospital not uncommonly undergo as many as 20-30 diagnostic tests, and many of these tests may be repeated on several occasions. A seriously ill patient or one who has been subjected to a major operation may receive 20-40 different drugs in addition to numerous mechanical procedures. His management may actually require use of anesthetics, sedatives, narcotics, antibiotics, arterenol, digitalis, diuretics, steroids, transfusions, infusions, antihistamines and much else either for the correction of symptoms of his disease or to combat the toxic manifestations of other drugs.

Since such combinations of measures and medicines are frequent it is not surprising that iatrogenic disturbances are frequent. Barr[1] encountered five per cent major toxic reactions and accidents consequent to diagnostic and therapeutic measures. Many took place before admission to the hospital and was the occasion for hospitalization. Others developed in the course of diagnosis and treatment in the wards. Some may have been missed.

Schimmel[2] also found about five per cent of major toxic reactions but when he included other "episodes" the incidence rose to 20 per cent of over 1,014 patients with 1,252 admissions. To be sure 110 of the 240 episodes were "minor" but 82 were "moderate" and 48 were major of which 16 ended fatally! There were 29 reactions to diagnostic procedures of which 13 were major and four died. There were reactions to therapeutic drugs in 103 patients with four deaths. There were 31 reactions to transfusions in 24 patients. Acquired infections occurred in 21 patients of whom six died. This then can be considered to be the cumulative risk to a patient who accepts the whole of our medical therapy. Schimmel did not include in his survey various toxic manifestations of drugs administered if the signs were deliberately invoked as guides to therapeutic dosage. Also excluded from his study were potentially harmful situations that were detected before noxious effects developed. Examples are hypoprothrombinemia occurring during anticoagulant therapy but without hemorrhagic manifestations, or asymptomatic replacement of bacterial flora of sputum or stool by staphylococci or monilia in patients receiving broad spectrum antibiotics.

These accidents, risks and dangers may be regarded as the price that we as responsible physicians must pay for the inestimable benefits of modern diagnoses and therapy. They are hazards to which with the best intent and most correct practice we occasionally subject our patients. Having said this aspect of medical practice, it is clear enough this risk is offset by our recognition of the triumphs of modern diagnosis and therapy, of the quick cures, the early restoration of health and vigor, the prolongation of useful life of our patients who are living evidences of the triumphs of our modern medical and surgical practice.

This problem is far from new. Medical history is replete with evidence of risks involved. We have lived through an age of nihilism when most useless drugs and procedures were abandoned and when Osler could find only a dozen or so for detailed study. Even then mercury, a good drug then, was known for its toxic effects. Slight overdosage of digitalis, so helpful in dropsy, was responsible for frequent discomfort and occasional sudden death. Many therapeutic measures were later recognized as futile and hazardous. Some of us can recall the cruel outdoor treatment of pneumonia, the cold baths for typhoid, the starving of fevers, the withdrawal of water or blood in cholera.

The many reactions encountered are important to bring to the medical profession. It brings us to the realization that we must hold all measures in some degree suspect. It will help us to recognize dangers if we realize that each new drug or procedure bears potential hazards that may not be immediately apparent and may only be discovered later when much damage is done. What lesson we have to learn from the above reports is that the probable benefit of each test or treatment must always be weighed by the physician against the possible risk. If we recognize the variety of dangers intrinsic in medical practice today then we will become more discriminating in our selection of measures, more reflective in our approach to our patients.

We will become more useful to our patients when we know when not to treat as when to treat. We will avoid potentially dangerous agents for trivial or inconsequential complaints. We will grow in discipline and understanding. By being aware of the hazards we as physicians will avoid unnecessary harm and minimize the "price we and our patients pay for modern management of disease," for a judicious selection of diagnostic and therapeutic measures can be made only with knowledge of these potential hazards as well as the expected benefits.

Moser[3] has called the "hazards" of Barr and the "episodes" of Schimmel diseases of medical progress, diseases that would not have occurred if sound therapeutic procedures had been employed. In Medicine as in every field of human endeavor progress creates problems.

L.H.N.

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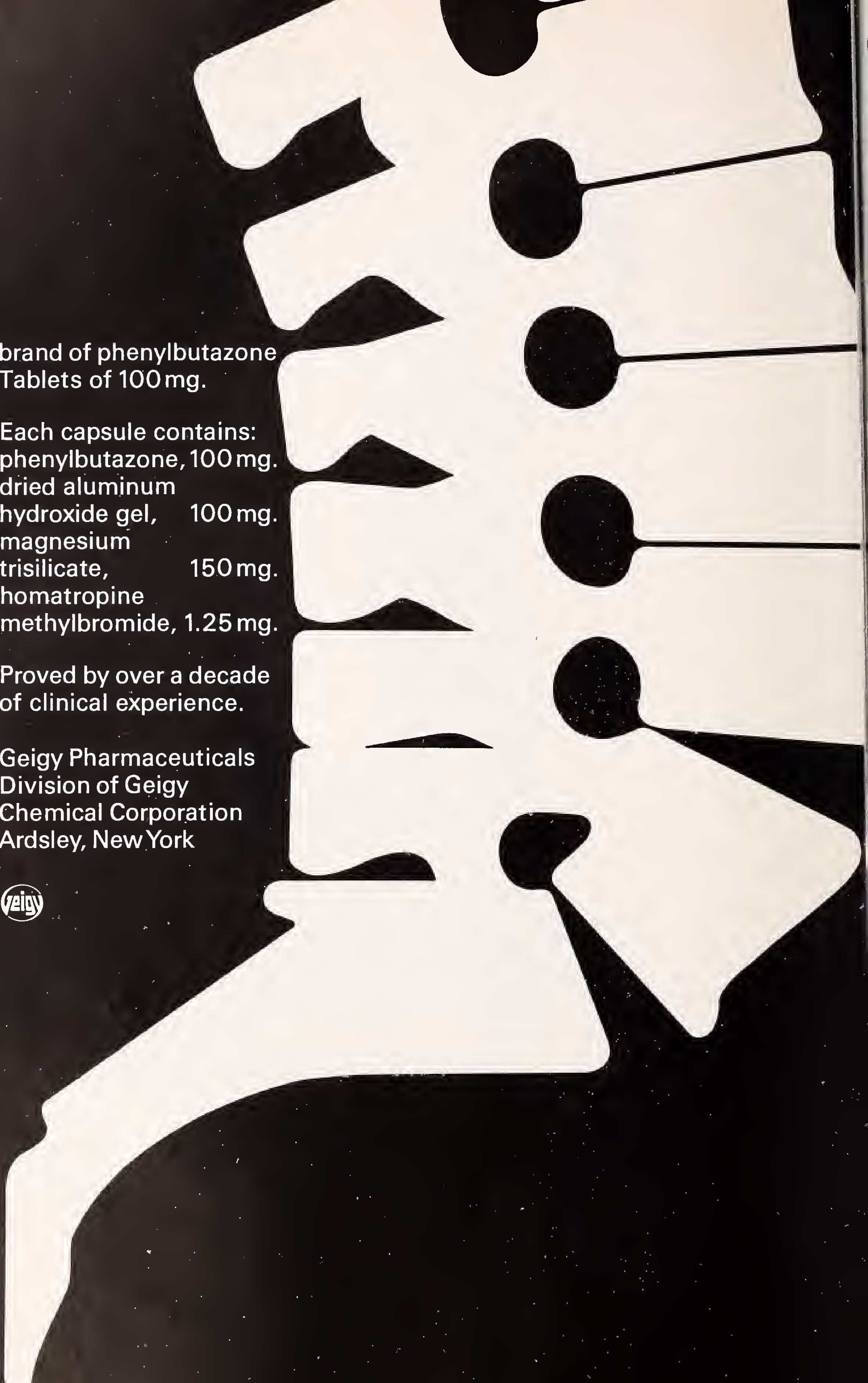

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Chemical Removal Of Nucleus Pulposus

Over six years ago, Thomas[1] found that intravenous injection of papain produced collapse of the ears of young rabbits. Not only the cartilage of the ears but all cartilagenous tissues of the body was also affected and the epiphyseal cartilages appeared to be particularly sensitive. If enough of the enzyme was administered the animals showed softening of the tracheal cartilages to such a degree that some animals died of respiratory obstruction. Apparently the changes occurring in cartilage after intravenous injection of papain were the result of widespread breakdown of chondromucoprotein.

This apparent selective action of papain on cartilage suggested to Smith[2] the interesting possibility of using such an enzyme for the chemical removal of the nucleus pulposus of protruded or extruded intervertebral discs. obviously any method of treatment must be accomplished by enzyme levels which are not capable of damaging surrounding tissues such as bone, ligaments, nerve roots, skeletal muscle and dura mater. Inasmuch as the clinical signs and symptoms associated with herniated discs can be relieved by the surgical removal of as little as 10 per cent of the total disc cartilage, only small quantities of a highly specific enzyme would be needed.

After studying the effects of various papain fractions in vitro in combination with cartilage powder, papain protease was found to be the most active, being several times more so than chymopapain in dissolving cartilage. In vivo, however, papain protease and chymopapain were not much different in their action. Smith *et al*[2] found that the degree of nucleus pulposus dissolution after six days was related to the dose. It was completely removed by doses of 0.156 mg./disc. With such doses the interior of the disc was dry with only a small amount of residue. To dissolve the annulus fibrosus 0.5 mg./disc was required. When the disc was dissolved, it led to a greater degree of mobility of the spinal column at the level of the injected disc and all animals appeared to be normal during the five to six day post-treatment period. However chymopapain was found to be highly toxic if injected into bone or intrathecally, and this appeared to result from proteolytic dissolution of the poorly supported capillaries of the arachnoid and pia mater. It had no effect on the conductivity of electrical impulses by nervous tissue when frog and rabbit sciatic nerves were exposed in situ. Neither functional nor histological alterations were observed.

These results indicated that chymopapain can effectively remove nucleus pulposus when injected into intervertebral discs of adolescent rabbits without apparent effect on surrounding ligaments, bone, nerve roots and dura mater. Accordingly Smith applied the technique to twenty-two dogs with paralysis of the hind legs believed to be due to herniation of intervertebral discs. He injected 1-5 mg. of chymopapain directly into the discs apparently involved, and fourteen of the twenty-two recovered to the extent of being able to stand or walk, and of the seven unimproved, six were found to have herniation or extrusion of the discs at levels other than those injected. In none of the animals were there present deleterious effects of the enzyme.

With such favorable experiences as a foundation, clinical trials were started in July 1963 on humans with sciatica secondary to herniated intervertebral discs.[3] All patients were in the category of operative cases in that they each suffered incapacitating sciatica which had not been relieved by other measures. Each patient had positive clinical findings indicating a protrusion or extrusion of a herniated lumbar intervertebral disc. Six had already undergone laminectomies with only temporary or incomplete relief of pain.

The patients had general anesthesia and needle placement was confirmed by AP and lateral X-rays and a discogram was done with a 50 per cent solution of sodium diatrozoate. Then chymopapain dissolved in normal saline was injected in volume 0.4 to 1.0 m.l. in two levels in units varying from 4-16 mg. Seven out of ten patients were rid of their sciatica and back pain six to eighteen hours after injection. One, not relieved, was found to have a small fragment of fibro cartilage infringing on the nerve root. Another patient who was relieved after injection suffered from sciatica when up and around. This gradually subsided and the patient was able to return to work in one month. One patient actually suffered accentuation of his sciatica for twenty-four hours, but then the sciatica and back pain disappeared, but returned at 50 per cent of its previous intensity when he resumed ordinary activity.

All patients described the presence of various degrees of stiffness and soreness in the low back after injection like a "Charley horse or stiff neck." The degree of soreness was mild in eight and severe in two and was commonly described as located at one or both posterior superior spines of the ileum and the side involved bore no relation to site of the injection nor even the side of the sciatica. The duration was usually a week or ten days. The pain probably was due to the settling of the articular facets secondary to narrowing of the disc spaces.

Obviously a new method of treatment for the chronic recurring and often puzzling condition of herniation of the nucleus pulposus needs time and large numbers of patients before an adequate evaluation can be made. Smith's experiences with his now forty cases have shown much promise for this method.[4] Since the experiments were successful in rabbits and dogs, the method offered promise for man also. Perhaps better enzymes than chymopapain will in time be developed. However, on the basis of Smith's well documented observations on man it appears that chymopapain injected into an intervertebral disc will relieve the signs and symptoms caused by herniation of nucleus pulposus from that intervertebral disc.

This story of the use of an enzyme to remove the nucleus pulposus is interesting as a phenomenon of biological research. The first observation was an accidental observation of Thomas. It was a basic science study without any idea as to what it might lead to. The results lay dormant for five years until they suggested to Smith a practical use of Thomas's results. Basic science and practical medicine certainly cannot and should not be dissociated.

L.H.N.

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The Nerve Growth Factor (NGF)

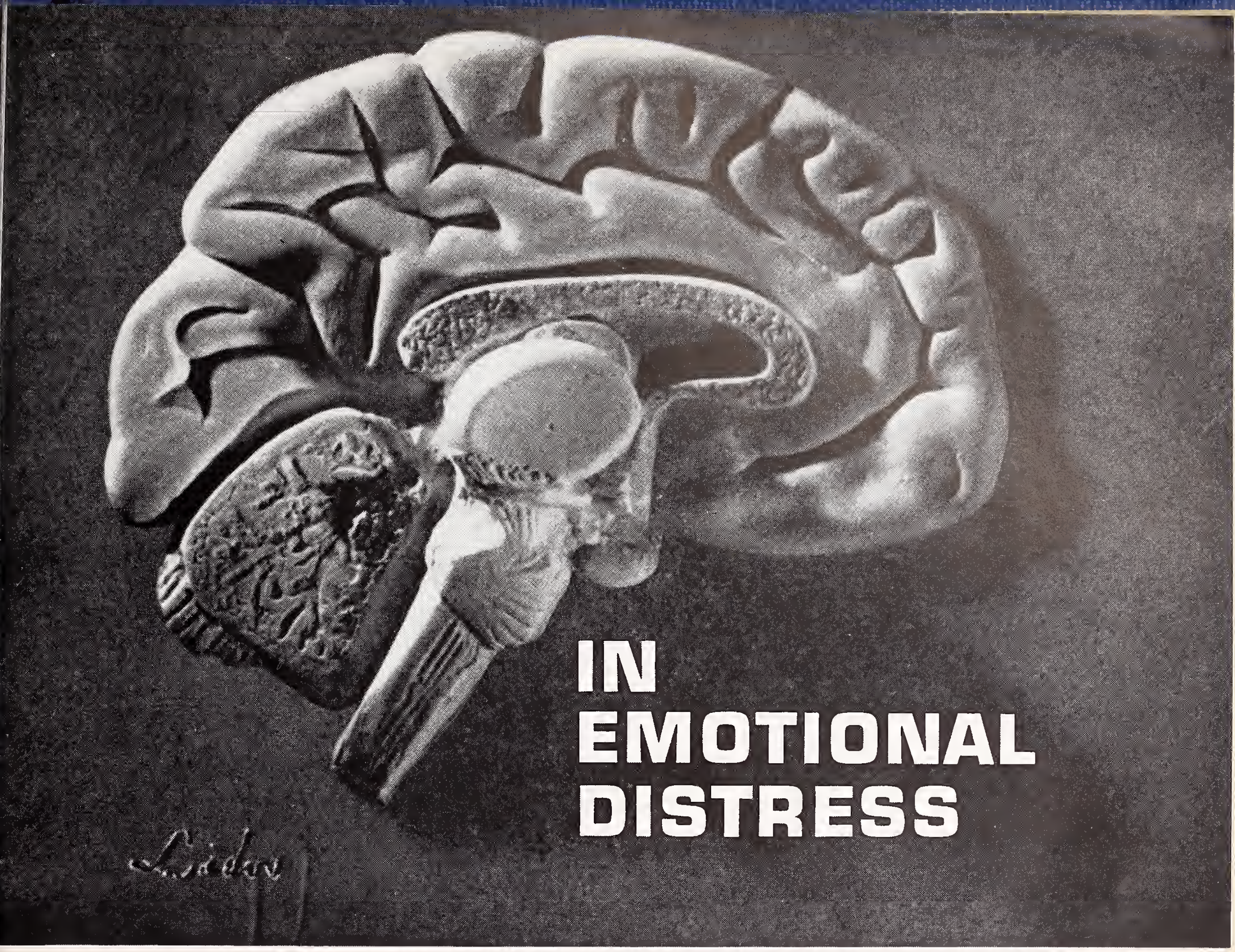
We are habitually confronted with observations that should cause us to pause and ask some questions. When a piece of skin is lost, quickly the adjacent skin undergoes mitotic division and regeneration proceeds apace. What makes the skin do this? When a portion of liver is removed, regeneration immediately starts and the lost portion is again restored. Here not only parenchymal cells regenerate but so do their vascular channels, lymph channels and bile ducts. Here the stimulus for regeneration involves a variety of structures not just the parenchymal cell. How do these tissues know when to start growing, how big to grow and when to stop?

We are now coming into possession of knowledge from embryogenesis that begins to give us a glimpse of the complex processes involved but also of the agents that participate in growth and differentiation. Take for example the nature of a developing nerve cell, whose aim is to establish contact with other cells such as muscle fibers, ganglion tissue or other nerve cells. How are these close morphological and functional connections achieved? By what bonds are the lives of these two partners interlocked? What would happen if such links were broken? A closely timed study of the response of sensory ganglia when a limb bud was extirpated in two days chick embryos[1] gave evidence of a sharp decrease in the mitotic activity of ganglia destined to innervate the amputated limb rudiments. The dividing cells of the ganglia lack any differentiative mark, and have no fiber connection with the periphery. The removal of the limb bud was not therefore a direct but a remote effect formerly designated by the non-committal term "field effect." In this situation not only does the adverse effects of amputation reduce mitotic activity of the sensory cell population, but the population itself is severely affected by a destructive process in which over half undergo sudden death and the surviving cells undergo regressive changes although they survive till the end of the incubation period.

This massive disintegrative process raises the question whether death of these cells might not follow the depletion of some agent essential to growth and differentiation of these nerve cells. Why should ganglia cells deprived of their end organs or peripheral field of innervation atrophy?

When the same ganglia are confronted with the task of providing the innervation of an additional limb bud, the mitotic activity sharply increases in these ganglia and all subsequent developmental steps from early to advanced differentiative processes are likewise enhanced. Such observations suggest that the periphery releases some agents which control the mitotic activity as well as differentiation in the sensory nerve cells, associated with these end organs. What can these agents be? The answer to this question came from a fortuitous discovery by E. Bruecker in 1947 who implanted a fragment of a mouse sarcoma 180 into the body wall of a two day chick embryo. He reported that nerve fibers from the adjacent sensory ganglia entered into tumor. The ganglia underwent a moderate increase in size of about the same degree as that resulting from the implantation of an additional limb bud, but it was only the sensory ganglia that connected with tumor through nerve fibers. How did the nerve fibers sense where to grow and how did the ganglia cells sense this need?

Levi-Montalcini re-investigated[1] this tumor effect, threw new light on the phenomenon and pursued it so that finally it led to the identification and isolation of a nerve growth factor NGF which was responsible for it. He observed that the growth



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response of the sensory ganglia contributing fibers to the tumor appeared two to three times greater than in controls. In addition the growth response of the sympathetic ganglia adjacent to the tumor appeared in fact to be five to six times larger than controls. So stimulating was the tumor to the sympathetic ganglia, that atypical ganglionic conglomerates were scattered in the tumor on the fringe of the neoplastic mass and the viscera, the ovary, spleen, thyroid and mesonephros tissues which normally do not receive sympathetic innervation until two weeks later. Thus was born the hypothesis that the tumor harbors a growth factor which selectively enhances nerve fiber outgrowth from the sensory and sympathetic ganglia of the host. When the tumor was implanted onto the chorio-allantois membrane the same phenomenon was observed. Here the tumor and embryo only share the same circulation. This was decisive evidence that there was released into the blood stream a nerve growth factor NGF produced by the neoplastic cells.

If this were so, then it should be possible to isolate and identify the active agent. The author then resorted to the tissue culture technique in order to test the effects of the tumor directly on isolated sensory and sympathetic ganglia. The results were so similar, that he proceeded to concentrate on this technique even though "the picturesque and esthetically attractive features of the embryological research was lost." But the investigation gained in precision and depth since it led to a chemical approach to the problem. The NGF became available in a purified form in large quantities and it was possible to assay its effects on the living organism and once again the embryos and the new born animals resumed their roles as the major objects of the investigation.

It is the rule rather than the exception in biological research that new leads often come from accidental findings and when these leads are followed, the investigation is often channelled in a new direction. In 1954 Cohen succeeded in isolating a nucleoprotein from sarcoma 180 and 37 endowed with the growth promoting properties of the tumors and their extracts. The question now arose whether the NGF resided in the intact nucleoprotein or a protein component of it. He knew that snake venom contained an extract that could lead to degradation of the nucleic acid component of the active fraction and so he added it to the culture media in minute amounts. To his great surprise he found that the snake venom itself harbors a NGF. In fact, ganglia cultured in a medium containing the purified venom at a concentration of 0.05 UG per m.l. developed an exceedingly dense halo of nerve fibers.

This unexpected and startling observation prompted a search for the venom effects in the living embryo. The results showed a striking similarity between the tumor and the venom effects. The only difference was that the specific activity of the venom is in fact about 1,000 times higher than that in a tumor homogenate and the only reason that the intact tumor evokes the growth effects in spite of its relatively low content of the NGF is because it is continuously releasing this factor by living and actively dividing cells.

While the discovery of the growth promoting factor in snake venom could not be anticipated, the finding of a similar factor in the submaxillary salivary gland of the mouse was the result of direct reasoning and planned research. Since the mouse salivary gland is in some respects homologous to the snake venom glands Cohen was led to search for another possible source of NGF in these glands. The experiments in vitro fully confirmed this guess. The NGF of the mouse salivary gland was 6-10,000 times higher than the specific activity of the tumor and about ten times higher than that of snake venom. The active substance was identified by Cohen as a protein particle with a molecular weight of the order of 44,000.

The next step was to test its effects in mammals. Sure enough, daily injections of the NGF in newborn mice in very small amounts evoked a striking increase of sympathetic ganglia already apparent forty-eight hours after the first two injections. After two to three weeks the same ganglia are four to six times larger than the controls, while no changes are apparent in the parasympathetic and sensory ganglia nor in any other nerve cell population. The cell measurements and cell counts show that the NGF calls forth an increase in the cell numbers as well as an increase in the size of the individual nerve cells, but the increase in size occurs only after the mitotic activity comes to an end.

This phenomenon apparently is universal since the effects of NGF was verified by in-vitro experiments on ganglia of several species, man included. Ganglia explanted from human fetuses which became available from surgical abortions show the same growth response to the N.G.F. as do the ganglia of birds and rodents. Apparently this protein is essential to the life of the target nerve cell for when sensory and sympathetic nerve cells are dissociated through trypsinization and explanted in liquid media, the cells will disintegrate unless NGF is added to the medium.

Out of these beautiful experiments of Levi-Montalcini and his colleagues there begins to emerge a grand design of a most important element in growth and differentiation. The N.G.F. is specific only for sympathetic ganglia and sensory ganglia growth. We are entitled to believe that all tissues embryonic as well as post-natal depend upon a specific substance probably a protein which promotes their growth and development. It is not too fantastic to look into the future and imagine that someday the substance or substances involved in the growth of the cerebral cortex will be discovered and then human evolution will take a long stride forward by the development of an enlarged cerebral cortex.

L.H.N.

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Find Newborns See Better Than Previously Supposed

A newborn baby has greater visual acuity and coordination of eye movements than previously supposed, Los Angeles researchers said recently.

Two studies of infants averaging one to two days old were reported by Glenn O. Dayton, Jr., M.D., Margaret H. Jones, M.D., Barry Steele, Marvin Rose, Patrick Aiu and Richard A. Rawson, M.D., in the current Archives of Ophthalmology published by the American Medical Association.

Estimates of visual acuity at birth have ranged from 20/2,000 to 20/670 and the development of normal 20/20 vision has been believed to evolve during the first five years of life, the authors pointed out.

However, in a study of 39 full-term, apparently normal infants, nine demonstrated 20/150 vision, according to the report.

The technique used was one which has been established for determining visual acuity in adults. It was performed by means of a canopy placed over the baby's bed. Eye movements were recorded electrically.

The records of only 13 of the infants could be interpreted because the others did not respond, some because they fell asleep.

The researchers concluded that the visual acuity in newborns is "at least 20/150 and may be even better." Not only the motor but also the sensory capacity for coordinated eye movement may already be present in the newborn, they said. Only infrequently were dissociated eye movements observed, they added.

Having determined that some newborns have sufficient visual acuity to fix both eyes on a single target, the researchers tested a group of 45 full-term, normal infants on their ability to follow a series of dots moving across the canopy.

Seventeen of the infants, the majority of those whose eyes were open during the test, were capable of locating the moving dots and following them across the canopy, they reported.

Each eye moved simultaneously in the direction of the target, they said, and both eyes moved over the same period of time. Tracings of the individual eye movements were similar indicating close conjugation of the eyes.

The study documents a fixation reflex which is innately better developed than heretofore reported, with the ocular movement purposeful and well coordinated rather than aimless and unconjugated, although not as smooth as in the adult, the authors commented.

The study was made at the University of California, Los Angeles, The Center for the Health Sciences.

Viral Interference Suggested In Measles, Chicken-Pox

A seven-year-old boy who unluckily had chickenpox and measles at the same time has provided medical scientists with an interesting view of what happens when two viruses clash.

The case was reported by Drs. Vernon Knight, William F. Fleet, and David J. Lang, National Institutes of Health, Bethesda, Md., in the current *Journal of the American Medical Association.*

The boy fiirst came down with chickenpox and one week later contracted measles. When the measles rash began, it was observed that the crusted healing blisters of chickenpox were surrounded by zones of apparently normal skin completely free of measles rash, according to the article.

This suggests "some type of interference between the two viruses," the authors said, and indicates that the virus of chickenpox and probably that of measles are present in the skin.

The researchers theorized that the interference of chickenpox with measles rash could be due to interferon, a substance produced by a cell when it is infected by a virus which provides resistance to viruses in general.

"The case in favor of interferon is that, although production of interferon by chickenpox virus has not been reported, interferon has been stimulated by practically all viruses which have been studied, interferon has been seen in the skin of guinea pigs infected with vaccinia virus, interferon is characteristically localized around the site of viral infection, and virtually all viruses which have been studied are inhibited by sufficient quantities of interferon," they said.

The Why's Of Quackery

Austin McCawley, M.D.

■ Stephen Leacock tells this story: "Years ago when I first got my Ph.D. degree, I was inordinately proud of it and used to sign myself Dr. Leacock, in season and out. On a trip to the orient I put my name down that way on the passenger list of the liner. I was just getting my things straight in my cabin when a steward knocked and said, "Are you Dr. Leacock?" "Yes," I answered. "Well, the Captain's compliments and will you please come and have a look at the second stewardess's leg?" I was off like a shot, realizing the obligations of a medical man, but I had no luck; another fellow got there ahead of me. He was a doctor of divinity."

One can laugh at Mr. Leacock's ambition to treat the second stewardess's leg, but there are those who assume the role of doctor and attempt to treat the human ills for reasons which are less amusing and more destructive to their fellows. They are often called "quacks," a name which they originally earned as itinerant medicine men who sold remedies of questionable value. From their glib speech with its barnyard overtones, the name "quack doctor" developed and also the name "quacksalver."

The history of quackery is an astounding one and its recitation must, like Eramus, stand in praise of folly. Some of the more ludicrous examples are ancient history, but others took place yesterday.

Elisha Perkins, who was born in Norwich, Connecticut, lived two hundred and fifty years ago and cured all types of diseases with two small pieces of magnetic metal. That is, they were alleged to be metal and magnetic. He claimed he could pull disease from the body by magnetic attraction. After his death, his son took the system to England where he was exposed by a Dr. Hygarth who resorted to the simple expedient of cutting into the tractors with a pocket knife. They proved to be two sticks of painted wood.

Two other practitioners from Connecticut, Doctors Fitzgerald and Bowers, believed that the body was divided into ten zones. Each zone originated in a finger and ended in the corresponding toe on the same side of the body. Disease could be cured by exerting pressure on the proper finger or toe or other area within these zones. For example, dandruff could be cured by rubbing the fingernails together and goiter required pressure on the first and second fingers. Their book *Zone Therapy* appeared in 1917 and their theories were eagerly embraced by the naturopaths.

This cult, naturopathy, has no founder and encompasses hundreds of strange methods. It is hard to define the tenets of the cult or to find any common basis for its thinking, but the various schools do seem to have certain ideas in common. They dislike orthodox medicine and adhor drugs and inorganic substances. They use herbs, herbal products, vitamins, diet, natural remedies of various kinds, water cures, purgatives and colonic irrigation. They are often vegetarian. They absolutely reject the germ theory. In a case of appendicitis, the true naturopath might prescribe fasting for a few days, then enemas followed by a special diet. Bernarr MacFadden was an enthusiastic advocate of naturopathic beliefs in his publications, and at one time advocated curing cancer by diet.

It is hard to say how many naturopaths are still operating; perhaps there are no more than a few thousand. However, there are many mail-order pharmacies, supplying natural remedies, herbal products, and so forth.

One recalls Horace Fletcher, a naturopath, who said, "Nature will castigate those who don't masticate." He thought each mouthful of food should be chewed thirty to seventy times. There is certainly no harm in this idea but Fletcher made the most exaggerated claims for the beneficial results of chewing one's food properly.

He felt that it would make people younger and more vigorous. There are still some Fletcherites around. Some years ago a Sunday cartoon page showed a picture of a matronly wife returning from a lecture and saying to her husband, "And that lecturer said that if we all chewed our food properly, we wouldn't have all these wars."

The osteopaths have now given up much of their opposition to orthodox medicine and teach many, if not most, of the medical disciplines in their schools. However, an offshoot of osteopathy, is chiropractic. Chiropractors, like the osteopaths, concentrate on adjusting spinal subluxations, to which all disease is attributed, and, like the naturopaths, reject drugs and germ theory. They are given to

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using machines with imposing names, as for example, the electroencephaloneuromentimpograph. Its mechanism of action seems obscure. As the sage has observed, all the tribes of the earth love to have their backs rubbed, but it remains for the Americans to make a profession out of it.

Homeopathic medicine no longer enjoys the vogue it did. This is perhaps just as well, especially when one considers the rather unusual character of their pharmacopoeia which included drugs like lachryma filia (tears from a young girl), asterias rubens (powdered starfish), skunk secretion and powdered live bed-bugs.

Rather than try some of these remedies, it would be better to go back to Cohausen. In 1744, he wrote "Hermippus Redivivus" or "The Sage's Triumph over Old Age and the Grave" in which he advocated sleeping between young maidens as a remedy for disease and a measure to restore healthful vigor. There have been criticisms of the therapeutic altruism of this concept, but willingness to follow similar prescriptions has been demonstrated many times.

Doctor William Horatio Bates proposed an original theory of visual accommodation which he advanced without benefit of any scientific proof. He considered that the lens was not important in accommodation and that the eye accommodated to allow for distance by the action of two external muscles which altered the entire length of the eyeball. He felt that all refractive errors were due to defective action of these muscles, which in turn was caused by strain; the strain was caused by a condition of mind. His theory was quite opposed to all the established evidence of ophthalmology but it was beguiling up to a certain point, although a trifle obscure. To quote from one of his writings: "When he (the patient) comes to realize, through actual demonstration of the fact that he does not see best where he is looking, and that when he looks a sufficient distance away from a point he can see it worse than when he looks directly at it, he becomes able in some ways to reduce the distance to which he has to look in order to see worse, until he can look directly at the top of a small letter and see the bottom worse, or look at the bottom and see the top worse." This makes sense?

His theories were, of course, very attractive to those who would like to throw their glasses away. Curiously, many patients claimed they were benefited by his system of treatment and this is one of the difficulties in attempting to expose any system of quackery. There are always grateful patients who, no matter how shamefully they have been duped, will swear in some way they have been cured or helped. Gardner discusses one of the Bates' cases:

"In Bates' case, certainly there were some patients who probably did not need glasses anyway. But there were others. In one case an aged woman had glaucoma (a hardening of the eyeball) in one eye and 'absolute glaucoma' in the other, rendering it totally blind. She was shown how to palm. 'In just a few minutes the pain ceased and the eyeball became soft.' Through the blind eye she was able to read the top letter of the test chart. This is unquestionably the fastest 'cure' of glaucoma on record. How can such a miracle be explained?

"The answer is suggested in the next sentences. 'She was very happy and wanted to talk, which I encouraged her to do. She said she was living in a small furnished room and . . . had no one to look after her.' Such a patient — lonely, old, neurotic — has little to do except meditate on her infirmities. Often a new type of treatment, by a friendly doctor, will offer new hope and with it a great change in mental outlook. At the beginning, such patients will exaggerate the poorness of their vision and as the therapy progresses, if they have faith in its curative power, will exaggerate in the opposite direction. Later, this particular lady suffered a relapse and was visited in her room by the author, who writes: 'Her thin face was lined with pain . . . I began to talk to her about the days when she did not suffer . . . She began to palm . . . and became able to imaging a daisy waving in the breeze. I asked her to imagine that her body was swinging with the flower. She did this, and within a few minutes her pain left her and she smiled.' "

Bates was vigorously championed by many, including Aldous Huxley and Gaylord Hauser. He died in 1931 but the cult still survives. His theories are very dangerous when a patient has glaucoma, atrophy of the optic nerves, or some other ailment which needs immediate attention before it leads to blindness.

In the field of psychiatry, a tragic example is the case of Wilhelm Reich. His original contributions to psychoanalytic theory were noteworthy and laid the foundation for much later work of value. His courageous opposition to the Nazi Party in Germany must be mentioned, for he was one of the first to point out the insanity of that movement and its leaders. However, even in his earlier thinking there were flaws and gradually he began to evolve a theory which was either the flowering of genius and a very original genius, or else a systematized paranoid delusion, according to the way you look at it. You pay your money and you take your choice. He shifted his interest from psychiatry to the field of what he called bio-physics and claimed he had discovered orgone energy. This force seemed to be a sort of élan vital. It was nonelectro-magnetic, permeated all nature, was responsible for cloud formations and thunder storms and was the basis for sexual energy. It was blue in color. He invented a therapeutic box, technically called an orgone energy accumulator, which was made of sheet iron on the outside and organic material (wood or celotex) on the inside. (Perhaps it was the other way around). At any rate, the theory was that orgone energy was attracted by the organic substance and radiated inwards into the box. The energy was supposed to speed up healing, sterilize wounds and cure cancer in early stages; it was also good for colds and hay fever.

For years, ever since Lydia Pinkham, certain worthless tonics have enjoyed great popularity, perhaps not unconnected with the fact that they have a high alcohol content. Hadacol is very popular in the South. Groucho Marx, on his radio program a few years ago, interviewed the inventor, who happened to be a State Senator from Louisiana. When Groucho asked him what Hadacol was good for, the Senator gave an answer of startling honesty. "It was good," he said, "for five and a half million for me last year."

In all areas of the country, patent medicines do a billion dollar business. These drugs are touted and sold across the counter on the basis of the most extravagant claims; these claims are not justified by the known action of their ingredients, or else are gross exaggerations of whatever slight pharmacological effect they possess. The advertising is so overwhelming that one takes the exaggerations for granted, discounts them automatically as part of the human comedy, and forgets about the whole tasteless spectacle. But look again at what is going on in full view of the nation. Look at the new arthritis remedies which owe their usefulness entirely to the fact that they contain aspirin. Look at the cold cures; nobody can cure a cold. Look at the imitation tranquilizers which are being sold across the counter. The active constituent usually is an antihistamine drug—methapyrilene hydrochloride—as, for example, in the preparation Tranquil. This is also the chief agent in various sleeping pills—Sominex, Nytol and others. The manufacturers do not stress the fact that only a small percentage of all people are sedated by antihistamines —less than 20 per cent.

The condition of obesity is a dripping roast for the makers of patent medicine. There are drugs to stimulate metabolism, depress the appetite, or flush fat off, soaps, pastes, girdles, belts, spot reducers, laxatives, cigarettes, chewing gum, and other agents, all of them ineffective and some of them forbidden to be sold through the mail. Some across-the-counter drugs advertised as curbing appetite contain phenylpropanolamine, which is not only present in quantities inadequate to depress appetite, but is also dangerous to some people in larger doses. One example is Regimen.

And so on—the list is endless: Abrams and his electric machine, Graham's magic bed, John Brinkley and his goat gland grafting, which he claimed would restore youth, Harry Hoxsey and William Koch with their worthless cures for cancer, Capon Springs water, phoney arthritis remedies, royal jelly, which appears to have no more active ingredient than the B complex vitamins, but is sold as the answer to the age-old quest for the Fountain of Youth, overpriced and overadvertised vitamins, ineffective cold medicines, false reducing pills, pseudotranquillizers, deceptively promoted and hazardous laxatives, bogus skin treatments, expensive and ineffective vitamin and hormone creams, deadly cancer cures—Why? Why do people fall for it?

Voltaire said that the quack was born when the first knave met the first fool. But it is really not quite so simple. Axel Munthe tells the story of how in Naples, some years ago, the authorities cracked down on the many quacks in town and required them to publish their credentials. One man refused. When the authorities investigated, they found he actually had very excellent degrees from first-rate medical schools, which would have qualified him to practice as a specialist in any hospital in Europe. They could not understand why he preferred to pose as a charlatan and conceal his medical background. "Because, he said, "my patients want to come to a quack. They come looking for something unusual and I give it to them. I have a very lucrative practice.

This story does reflect one part of the problem. Certainly the Almanach de Gotha and the Social Register could be used as listings of many who resorted to quackery. The gullible are often bored and seek vicarious outlets. The desire to become an initiate and be among the first to recognize a new genius, the wish simply to escape from boredom, and maybe even the urge to try and beat the system, can all be motivating factors in those who seek treatment from the quack. Some people spend their lives trying to beat the system.

It might be amusing if these measures did not mislead the helpless, the inadequate and the poor. Also gullibility is only one reason why people resort to these unscrupulous dispensers of unhappiness. They are driven by fear, desperation, ignorance, the desire to escape from the inevitable, and the need to deny the realities of illness.

Under stress, the human psyche resorts to various defense operations or defense mechanisms to avoid the burden of an anxiety beyond tolerance. Among the most primitive and ineffective of these defenses are denial and magical thinking.

A man, who suspects that he has a serious illness, panics, denies that there is anything wrong, and avoids the doctor who might find out otherwise. He denies he is ill and seeks a practitioner who will tell him what he wants to hear or one who will perhaps treat him without the necessity of the surgery he fears.

A man who cannot with equanimity accept the burden of advancing years and look for the normal satisfactions of age, denies the inevitability of the passing finger, seeks the magical cure that eluded Ponce de Leon, and spends 306 dollars on a "magic spike from Vrilium Products Company of Chicago. The salesman assures him that its rays will make him 20 years younger.

In every resort to quackery, the petitioner attempts to attain something out of the ordinary, that is beyond common experience, against the rules, contrary to average fact and a refutation of the inevitable.

Patients turn from natural law and seek supernatural help. There are many faith healers in this business and it is regrettable that they are so relatively free from criticism because of the immunity of their cloth. But in the resort to any quack, whether or not he is a faith healer, there is an element of the appeal to the supernatural and an abandonment of the logical and natural order. The tragedy is that, unless the condition is minor, the patient must eventually face the bitter reality of disillusionment and an illness which has progressed without adequate treatment.

A middle-aged man comes out of a chiropractor's office in New York. He has had some back pain for a while and has had several gastrointestinal upsets with some blood in his stools. He doesn't really trust doctors—they are too quick with the knife—but it doesn't matter now. The chiropractor has assured him he has a subluxation of the eighth thoracic vertebrae which can be corrected with a course of manipulation. For him the future holds the reality of an inoperable carcinoma of the colon. He suspects this and is driven by fear.

A young girl in her 20's stands outside the office of a dianetic auditor, a practitioner of Dianetics. She has been having emotional difficulties for some time, is unable to work, depressed, anxious and suffering from many phobias and psychosomatic symptoms. She has had some other symptoms which she hasn't told anybody about, and doesn't intend to, including the auditor who has already seen her in 15 hours of therapy. But everything is going to be all right. She has had all her engrams removed and should soon be a "release" whatever that means. It really is wonderful, she tells herself, to realize how early impressions before birth, like hearing what her father said to her mother at the third month of pregnancy, could effect her whole life and cause her to be ill for years afterwards—a not unusual dianetic interpretation—well worth a thousand dollars.

This girl is on the verge of a serious breakdown and any competent psychiatrist would treat her with great care. She may be pushed into psychosis by her dianetic treatment. For the psychiatrist who treats her then, all that junk about removing engrams is going to be very difficult to unravel.

Consider a woman in her late forties—She has always been rather nervous but she married young and in the press of bringing up a large family, never had time to think about it, or do much else for that matter. The youngest went to college a year ago and, all of a sudden, she was at loose ends. She doesn't know what to do with herself, that is if she felt up to doing very much. Recently, she has had some bad health. She feels depressed and has experienced severe back pain and frequent headaches. Her doctor told her that there was nothing physically wrong but the trouble was emotional. She didn't believe that so she found another doctor. He was recommended by a friend and is not a regular M.D. But he seemed sympathetic. He treated her back pain with manipulation and massage. Recently she has been having stomach pain and he placed her on a special diet. She feels better.

With the sympathy and attention she is getting, she will feel better for a while. But as soon as one symptom or "disease" is cured, she will have to be treated for something else—until her money or her patience runs out. Then she will still have her symptoms, and the situation she cannot handle in her personal life will still be there unfaced and unresolved.

The difficulty in prosecuting these traffickers in human suffering is that they all find patients they can heal and who will testify for them in court. This happens for several reasons. Many human ills run their course and get better without treatment of any kind. Then many ills are psychosomatic and of a kind which responds to supportive therapy, a sympathetic listener and encouragement. The danger is that if the underlying condition is serious the patient is prevented from getting adequate treatment. When psychiatric problems exist and there is no physical disease the patient may benefit temporarily from attention but the quack is unable to evaluate what he is doing and in the more serious emotional disorders great damage may be done.

The placebo effect is the weapon of the quack. The placebo is a medicine given to please and the patient benefits from it for psychological reasons, without any pharmacological justification. Placebo effects are not imaginary. They influence principally subjective complaints, although the physiological effects can also be startling. For example, some investigators have produced eosinophilia with placebos, a rather unusual finding. This particular experiment brings out the fact that there is more than suggestion involved although it is certainly a factor and suggestible patients show a stronger placebo response. As no pharmacological activity is involved, the action must be through the interpretive areas of the brain and then the effect may be mediated through nerve channels and autonomic pathways to the end organs. The attitude of the physician is all important in influencing the character of the response.

Although this mechanism has been recognized for a long time it has only been studied to any extent over the last few years. Stewart Wolf presented a fascinating paper on this subject at the 1957 meeting of the Association for Research in Nervous and Mental Disease. He says: "Our own experiences with the toxic effect of placebos included a study of the reported anxiety relieving effects of relaxant drugs . . . it was found that the results with the drug and placebo were almost identical. Many of the patients noted minor toxic effects including drowsiness and sleeplessness, nausea, tremulousness, palpitation and so forth. The incidents of these minor side-effects was identical with both placebo and the agent. One individual developed dermatitis medicamentosa while taking a placebo. Another individual who had a severe collapse and anaphylactoid reaction with mephenesin had an identical reaction with the placebo." He gives one example which strikingly illustrates the importance of the physician's attitude: "The patient who had had chronic asthma for 27 years, had suffered almost continuous asthma for the past 17. He was a favorite subject on which to test new drugs. He had even become refractory to epinephrine. Finally, one product seemed effective. When he was given the agent, he was free of asthma; when it was stopped the asthma returned. Accordingly a placebo was substituted without the patient's knowledge. Asthma was not relieved. Shifts from agent to placebo and back again were carried out several times with consistent results in favor of the agent. When the company was approached for an additional supply of the material, the representative acknowledged that, because they had had so much trouble with positive enthusiastic reports, they had in this instance sent along the placebo first.

Obviously if the conditions are right, a placebo can exert a powerful effect. All physicians know this mechanism and are helped by it to some extent. But they do not rely on it; they know that placebos do not influence underlying disease. There is both an art and a science to medicine. The quack always makes himself an expert in the art and ignores the science to his patient's cost.

The cost is considerable in dollars alone, but the real payment is made in human suffering. It is an open question whether the unscrupulous operator is more dangerous than the fanatic who deludes himself as well as his customers. But the charlatan plays on human needs and manipulates the emotions of fear, desperation, loneliness and suffering; he makes his patients lose not only their health and money but also their dignity and their trust.

Much is already being done on the State and Federal levels to deal with quackery; much remains to be done. There are many excellent speakers in this program, well-qualified to discuss the enforcement of appropriate measures. A conference on such an important and such an unhappy subject is timely; it concerns us all. Let us hope it will lead the way to further constructive action.

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Quackery In Connecticut

Franklin M. Foote, M.D.

Promotion of highly questionable or ineffective means of treatment of disease is a source of much mischief, financial loss and sometimes outright harm. Being interested in the prevention of unnecessary disability and suffering we in the state health department are particularly concerned about the possibility of actual harm. Such harm may be produced because of the fact that victims of serious disease may be led to neglect effective methods of treatment, during the period of trial of a "quack" remedy, and thus the underlying disease process may advance and bring about irreparable damages may advance and bring about irreparable damage life.

With regard to the mischief that is not infrequently perpetrated, I recall less than three years ago a middle-aged lady who, on the advice of a taxi driver, consulted a Connecticut laboratory, about her symptoms, had a blood test taken, and on the basis of this test which several years ago was proved completely unrelated to the diagnosis of cancer, was told that she had cancer somewhere in her body. This lady became so apprehensive and upset that her physician had to admit her to a general hospital for several days, in fact, over the Christmas holidays, where she had a wide variety of clinical laboratory tests and X-rays, including stomach and colon. Only after thorough probing with almost every instrument that has been designed for insertion into all the body's orifices did she feel sufficiently reassured to leave the hospital for the security of her home. Perhaps the only damage done here was to the lady's nervous system and her pocketbook, as well as the unnecessary occupancy of a hospital bed during the Christmas season. However, it is good to know that the 1961 General Assembly enacted legislation that was signed into law by the Governor regulating clinical laboratories and making such an incident most unlikely in the future.

Not all the advocates of these will-o-the-wisps are easy to identify. Although not necessarily always slick operators, some that I have met are urbane and cultured, making an excellent impression on first acquaintance. Others appear to be a iittle uncouth, like a rugged man of nature whom one instinctively feels is obviously trustworthy, At least one frankly says that he does not claim to have a cure for cancer, it would be quackery to say this, he says. However, he declares that his preparation when injected offers hope and comfort to cancer patients, and can make the tumor regress.

Although many worthless disease treatments are the stock-in-trade of pseudo-scientists and promoters whose chief interest lies in turning a fast buck, it is embarassing to recall that some fairly well trained physicians, who should know better, occasionally become far too overly enthusiastic about some therapeutic method or advice which more sober researchers have found either worthless or harmful. Recent examples are the Vermont doctor, with his honey and vinegar treatment of arthritis, and the New York obstetrician who took in a tidy sum from his book, co-authored with a public relations writer, entitled "Calories Don't Count." The wrinkle clinic that operated for a short time in Westport last year, had as one of its associates in its early stages a fairly prominent New York dermatologist, since retired to Tennessee. His blessing of the 85 per cent carbolic acid treatment of wrinkles enabled his associates to achieve nationwide publicity in a picture magazine, and to soak their unsuspecting customers a fee of $750 to $1,500 per treatment. One of the Budkon Center's patients exhibited to the jury an atrophic scar above one eyebrow and another scar below the chin as a result of the process that she made the journey from Florida to Westport to obtain. Fortunately, Connecticut's hospital licensing and medical practice laws are so excellent that the center was closed promptly through the alertness of the state police working with our own staff. Three members of the corporation paid fines totalling $500, and the fourth, a beautician who elected a jury trial, was found guilty on all ten counts of practicing medicine without a license, received a suspended sentence of 300 days in jail and paid a fine of $1,000.

These instances as well as one of an unproved treatment for mongolism which contains not one or two but 57 scientifically balanced ingredients, show that we do have our problems in Connecticut. It is most gratifying, therefore, that so many of you are devoting an entire day to getting up to date on the current nature of the problem of quackery and how to combat it. I am most grateful to the state medical society for taking the initiative in organizing and supporting this most worthwhile session.

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The Unproved Method In Cancer Treatment

L. Henry Garland, M.D.

'Tis too much proved—that with devotion's visage
And pious action, we do sugar o'er
The devil himself.
Hamlet, III, 1.

■ The term "cancer" embraces an ill-defiined and heterogeneous group of diseases of widely variable natural history. Some types of cancer are very slow growing and only locally invasive or malignant. Others are very rapidly growing and beyond the probability of cure, even before a diagnosis is possible. Because of the variable nature of malignant tumors, there is sometimes difficulty in reaching a definite diagnosis, even with the microscope. Some conditions strongly resemble cancer, but ultimately prove not to be, and go on to spontaneous cure. Others which appear to be benign growths turn out to be cancer. These situations are usual, but they indicate the need for an adequate number of treated cases before a valid claim of a useful treatment method can be made.

A variety of drugs, sera, toxins and hormones produce temporary and occasionally dramatic improvement in the general condition of the cancer patient; some even temporarily arrest the growth of the cancer itself. These transient effects impress those who are unfamiliar with the peculiarities of the disease. From these facts, it is apparent that almost any proposed treatment for cancer can acquire some followers.

To establish the reliability of a method of treatment, it is necessary to subject a number of patients to the method or drug in question, and, if effective, to study their progress over a period of years to make sure that the apparent cure is sustained. It is impossible to make dogmatic statements on the validity of a claimed cancer cure until sufficient time has elapsed to permit fair evaluation of the results; nevertheless, ineffective methods are usually apparent as such within much less than a year.

The only reliable methods of cure for most types of cancer are surgery and radiotherapy. There are a few examples of unusual tumors which have been controlled for many months by certain chemicals, but by-and-large drug therapy can usually provide only temporary relief or palliation for the majority of human cancers.

Chemicals and drugs of various type are under continuous scientific investigation by groups sponsored by the National Research Council, the Federal Food and Drug Administration, the U.S. Public Health Service, the American Cancer Society and many individual scientific investigators. The Cancer Commission of the California Medical Association has, for the past fifteen years, invited the proponent of any treatment for cancer to submit the method, with proper documentation, for adequate trial by responsible, impartial investigators, with the understanding that the results of such testing, whether favorable or unfavorable, will become a matter of record. Any new treatment that proves to be efficacious would be a boon to mankind and should be fully supported. Conversely, worthless methods raise false hopes, cause a useless waste of money and divert patients from timely recourse to the only known effective treatment programs. They should be swiftly exposed in the public interest. It should be recollected that clinical trials on man are essential for the evaluation of agents potentially beneficial to man. Such clinical trials are regularly conducted, first on a preliminary basis and then on a larger scale. With adequate records, adequate controls, and adequate publication, scientific facts can be accumulated and the public ultimately benefitted.

Unproved Methods

Owing in part to the fact that some cancers are widespread and therefore incurable when first diagnosed, and in part to the fact that many lay persons shy away from radical surgery or radical radiotherapy, large numbers of the public are ready to listen to those who promise cure by methods not only unproven, but obviously fraudulent. Some forty years ago it was estimated that there were over four thousand promoters of cancer cures in the United States. There were even charlatan hospitals with complete staffs, large buildings and every appearance of sound fiscal backing. There were concerns which manufactured and supplied

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cancer cures upon a mail-order basis. The claims of these charlatans were heard and heeded not only by people with no knowledge of medicine, but unfortunately not a few licensed practitioners. These doctors used the cures in their practice just as they used scores of proprietary medicines whose sales depended upon the clever manner in which they were advertised.

The suppression of such frauds is difficult. It is hard to prove that some materials are without slight beneficial effects, at least psychologic. These observations were made in a report published by the American Society for the Control of Cancer some forty years ago. They remain true today.

Quackery might be described as the world's second oldest profession. It is certainly as old as recorded history. In the dark ages crystal gazers and stone cutters attempted to cure various mental disorders including presumably, brain tumors. These imposters made a superficial incision in the scalp and cast some previously palmed stones into a convenient receptacle at stated intervals during the patient's struggles. The trick is shown in a painting by Hieronymus Bosch, dated about 1500.

Some of these quacks give every appearance of respectability and authority. Three of them, dating from the early decades of the present century deserve brief mention:

Dr. L. D. Rogers was once the head and chief owner of the National Medical University of Chicago (virtually a diploma mill). He developed a cancer serum and organized the American Cancer Research Society, with none other than L. D. Rogers as president. His autohemic therapy consisted of giving his patient a solution made by "attenuating, hemolizing, incubating and potentizing" a few drops of his or her own blood, and administering it according to a refined technique developed by himself. He advertised mail order courses for other physicians to the tune of $100, wrote a book called "Autohemic Therapy," and organized the Autohemic Practitioners.

Dr. Arthur de Collard went one step better. He turned up in Richmond, Virginia, in 1918 and persuaded the Legislature to license him to practice Poropathy. He claimed to be a cousin of Napoleon and a graduate of several European universities, but unfortunately all of his diplomas had been accidentally burned. The bill defined poropathy and manipulative surgery as a new branch of therapeutics, by which innumerable diseases, including internal cancer, could be cured. By 1927 there were several Poropathists in the State of Virginia who had taken the course under de Collard.

Dr. Albert Abrams was professor of pathology at Cooper Medical College in San Francisco (the precursor of Stanford University Medical School). In 1916 he presented his new concepts in "Diagnosis and Treatment; Physiochemical Medicine" and founded the Journal of Electronic Medicine, himself editing the first six volumes.

The diagnostic technique consisted in placing a drop of the patient's blood in a box called a "dynamizer" containing a "jungle of wires, batteries and a rheostat." The dynamizer was provided with an electrode which was placed on the forehead of a healthy subject—often this was his chauffeur—facing west in a dim light. From areas of dullness elicited by percussion of the healthy subject's abdomen, Abrams attained the diagnosis of either disease or religion. If this sounds absurd, consider the therapeusis of sympathetic vibrations supplied from another box, the oscilloclast; as adjuvants, vividly colored ointments supposedly of a certain radio activity were smeared over the patient's abdomen. The oscilloclast was rented to all comers, physicians and others, at $200 to $250, plus monthly payments of $5 for each machine. It was not sold—only leased—with a definite understanding that the machine was not to be opened by the lessee. In a few pages of eulogy by Upton Sinclair, one reads: "The average charge is about $200 for a guaranteed cure of such diseases as syphilis, tuberculosis, cancer and sarcoma." The Scientific American, after a year's investigation, concluded: "At best it is an illusion; at worst, it is a colossal fraud." Abrams died in 1924 at the height of the controversy.

The Menace Of The Charlatan

From the above cursory review it is apparent that quacks are as old as human nature and as widespread as mankind. They vary from age to age like clothing fashions. Are they more of a menace today than previously? It seems to me that they are, because of the currently improved outlook for both the early and late case of cancer in the light of modern surgery, radiotherapy and chemotherapy. Their menace might be summed up as follows:

1. The unorthodox practitioner accepts patients with curable cancer and uses worthless remedies on them until the cancer becomes incurable. Not only is this evil in itself; it has the secondary effect of increasing the public's fear of cancer because of the evidence of one more uncured case.

2. On patients with late cancer, the quack often uses methods far less effective to control the disease and make life comfortable than are available by the use of orthodox methods.

3. Quacks often exhaust the savings of those in limited circumstances, without according any benefit—and even cause diversion of funds from responsible investigators.

Specific examples of wasteful methods included the Magic Spike which sold for $300, the Spectrochrome Lamp, rentable for $90, the Arginase Treatment, available to "terminal cases" for $600, and the Cancer Tonic Remedy, available for an initial fee of $400. Examples of diversion of funds included the notorious adrenal cortex extract treatment of the 1930's, and the lipid fraction methods of the 1950's.

Recognition Of The Charlatan

A charlatan has been defined as one with only superficial knowledge of his subject, who promises cures and who gulls the laity by hocus-pocus and other spectacular methods, frequently with complicated dials on chromium plated apparatus. He has also been defined as a medical fraud, claiming to cure disease by useless procedures, secret remedies and unproven therapeutic machines. Nevertheless, the spectrum of the quack is obviously broad. At one end are rather reputable members of the profession who are simply misguided or uninformed on cancer therapy, but who do not make a practice of seeking out cancer cases, nor charge exorbitant fees for the somewhat useless remedy they use. At the other end are the ghouls who operate what amounts to an assembly line, using methods they know to be useless and charging inordinant fees. The gross annual income of some of the latter is in excess of a million dollars; the harm they do to curable cases is incalculable.

What of the physician who uses orthodox methods, but in an incompetent fashion? For example, the surgeon who removes only part of a removable tumor; the radiologist who gives only part of a necessary cancericidal dose; the internist who uses only "a little" chemotherapy (when adequate treatment might mean the difference between failure and longterm palliation). These men are sometimes called quacks by their brethren, but they are not. They are the incompetent or unconscientious fringe which unfortunately prevails in every profession. The public can avoid them only by using thought, diligence and consultation.

Recognition of the charlatan is aided by noting the following:

1. His treatment or method of administration is available only from himself.

2. He uses press releases on the radio, TV or in the newspapers rather than scientific journals for his preliminary publicity.

3. He has no scientific controls to support the efficacy of his method.

The more flagrant quacks are recognized by the following additional features:

4. Many of the "cured" cases have no evidence of having cancer when treated.

5. Medical records are scanty or nonexistent.

6. Consultation with reputable physicians is discouraged or evaded.

Both types of charlatan tend to use the name of a high-sounding research organization or foundation. Both tend to be supported by quite outstanding citizens, often journalists, lawyers, writers, actors and even statesmen . . . but not persons experienced in the natural history of cancer or the care of patients with that disease. Following representations by some of these persons or by officially appointed investigators, it has been our experience that the proponent often promises to make some of his agent available for adequate trial. However, he seldom delivers the promised drug or drugs, making a series of excuses ranging from the fact that it is expensive to produce, to the fact that it can only be administered under his personal direction in order to be effective.

A classical example of the evasive technique used by one of the more notorious lay charlatans is as follows:

Mr. Hoxsey, a cancer clinic operator, had requested an evaluation by the National Cancer Institute of his therapy. The Institute asked him to submit at least fifty records of patients with internal cancer, diagnosed by a competent pathologist, and with a survival of at least five years after treatment. Sixty case records were received, of which, only nineteen were internal "cancers." Of these, only five had biopsy records, and none of these could be confirmed as cancer on examination at the Institute. The sixty case records were composed of forty alleged external cancers, nineteen of internal cancer and one of site unmentioned. The external cancers had biopsy data on only fifteen; the available slides showed no squamous cell lesions or melanomas; there were apparently a few basal cell carcinomas. In summary, two-thirds of the "cancers" had no biopsy at all; many of those which did have biopsy were not validated as cancer by the pathologist.

Investigation Of Remedies

In California, the Cancer Commission of the California Medical Association undertook in 1952 to investigate certain unorthodox cancer treatments which were gaining publicity in that state. The Commission functioned as a body of eighteen physicians, most with considerable clinical experience in cancer work and many on the teaching staffs of medical schools.

The Commission first prepared a carefully worded "Statement on Cancer Treatment" and issued such to over 700 newspapers and other public media in California. It invited the proponent of any treatment for cancer to submit the method of treatment, with proper documentation, for adequate trial by responsible impartial investigators—with the understanding that the results of such tests, whether favorable or unfavorable, would become a matter of record.

It then studied a series of alleged cancer remedies and published the results in the Journal of the Association (California Medicine). In these studies, the Commission was aided by the Bureau of Investigation of the American Medical Association, the Federal and State Food and Drug Administration, and the Committee on Cancer Diagnosis and Therapy of the National Research Council.

As soon as the facts were established concerning these alleged cancer remedies, the Commission made available suitable reports to the science writers of press, radio, and TV, and to the branches of the California Division of the American Cancer Society.

In performing each of its investigations, the Commission took the following series of steps:

1. *Ascertain the precise nature of the treatment method.* Frequently the method turns out to be an old one with a new name. For example, the Hepasyn treatment for cancer turned out to be Arginase (which had been previously investigated). Sometimes the nature of the treatment method is shrouded in mystery. It took quite a few months to find out that the material from which Dr. Gregory made his cancer treatment, Gregomycin, came from a mold in his back garden. The precise method of administering the drug, the dosage, the intervals, the side-effects and so forth are elucidated as fully as possible, both by conferences at the local level and much correspondence.

When we prepared to call on the proponents of the Laetrile cancer remedy (made by the John Beard Memorial Foundation) we found to our astonishment that there were two John Beard Memorial Foundations, at different addresses in San Francisco. The Foundations were not connected! The peripherally-located one housed our researcher; his laboratory consisted essentially of a small quonset hut in the back yard of a private house in which a vast number of empty ampules lay waiting to be filled with the chemical.

2. *Interview the proponents and review their scientific background.* It is sometimes difficult to secure personal interviews, but they have been obtained. It is usually simple to ascertain the scientific background and the record of previous publications. Every effort is made to give the proponents full opportunity to present all available facts.

3. *Examine the experimental evidence offered by the proponents.* This is not always easy; indeed, the amount of experimental evidence is often remarkably scant. All too often the "numerous laboratory animals" turn out to be a few mice or a solitary guinea pig. One of the researchers we called upon told us that he had method for producing transplantable adenocarcinoma of the large bowel in dogs; we were particularly interested in seeing this, but unfortunately the dogs were unavailable at the time of our visit; and the technique not written down anywhere. The experimental animal proved to be ectoplasmic.

4. *Examine the clinical evidence offered by the proponent.* An attempt is made, with the permission and cooperation of the proponent and the persons involved, to see and examine treated patients, to review the microscopic slides, the radiographs and other objective evidence, and if necessary, to make fresh sections from the blocks removed. All too often there is no microscopic tissue available. When it is available, it is often found that the entire tumor had been removed surgically or destroyed radiologically prior to inception of the cancer treatment method in question! An attempt is made to have at least one well qualified surgeon, radiologist and pathologist at such review sessions.

5. *Examine the autopsy data of the proponent.* (If any is available).

6. *Secure some of the drug for analysis and trial on experimental animals.* This proves much more difficult in practice than in theory. However, means are usually found to secure enough for at least initial analysis. Disillusioned former clients of the healer have cooperated in securing some of the material for examination. The laboratories and departments of chemistry of some of the universities in California have been very helpful in performing necessary tests.

7. *Treat a small number of patients* (persons beyond reasonable hope of control by established surgical or radiotherapeutic methods).

8. *Examine the autopsy data if any,* on patients treated under the auspices of the Commission or otherwise.

9. *Consult with other investigating groups and research workers.*

10. *Following these steps the evidence is summarized and reviewed by the Commission.* A report is prepared, cleared through legal counsel for the State Medical Association, and offered to the State Medical Journal for publication. If and when published, copies are transmitted to interested persons.

Steps To Reduce Charlatanism

The members of the medical profession who belong to the American Medical Association have supported the Bureau of Investigation and the Committee on Research of that organization for many years (the former now for over 50 years). The Bureau has compiled data on countless cancer frauds and worthless treatment methods, provided chemical analyses of hundreds of cancer drugs and remedies, and aided Federal and State bodies in exposing charlatans. But that is not enough to cope with the hydra of cancer chalatanism. It needs nine times ninety arms in the different parts of the country to keep pace with the sprouting heads. Some of those arms could be state or regional cancer commissions.

A Cancer Commission can, at the state or local level, investigate new or notorious cancer remedies, publish its findings and proceed according to the facts ascertained. If something apparently worthwhile materializes, the profession will be the first to study it—as it did in the case of insulin, the sulfa drugs, penicillin and other now-established agents. If, on the other hand, nothing worthwhile is disclosed, then the profession and the public should be informed. If members of organized medicine are reported to practice quacksalverism (that is, they continue to use for regular clinical cancer treatment, methods found by impartial study to be wortheless for that purpose), they should desist, and, failing compliance, should be asked to appear before properly constituted committees of their county medical society to show cause why their membership should not be terminated in the public interest. The kernels of this aspect of the problem are an actively functioning cancer commission (to establish facts), and a courageous local medical body (to take action on members who are defrauding the public). In the case of physicians outside the ranks of the medical society, it would seem that the state licensing body or state board of medical examiners should evolve a mechanism for effective action.

If and when the medical profession takes steps to correct the situation in its own membership, it can then with reason request members of other healing-arts groups to do likewise. Finally, it can go to the press, radio and television agencies with the documented facts on these efforts at public protection and request those bodies to lend their aid . . . so that quackery in non-professional spheres, that is, by laymen and cultists, may be curbed or reduced. The public needs and deserves frequent reminders that thorough scientific investigation of many cancer nostrums has been made — unfortunately without yet uncovering a more effective treatment for cancer than those already known.

In our own state, in a small way, we have made a few strides. As a result, at least three potential cancer cures have been deflated. In addition, one large Los Angeles daily newspaper rejected lucrative full-page testimonial advertisements from a notorious Colorado cancer clinic; at least one large broadcast service refused to relay a "planted" quack cancer-cure story; two worthless cures failed to obtain tentatively assigned research grants running into six figures; two members of organized medicine have been censured. And, on the positive side, we have succeeded (as have other states) in getting many press, radio and television releases on what the public should know and do to avoid falling into the hands of cancer quacks.

The public needs to be shown, as well as told. Science writers might agree to take the considered reports of the local cancer commission on a given cancer remedy and "show" step by step in lay language the type of investigation made and results. If there is a shred of hope in the proposed treatment method, the medical profession will have been the first to make further studies. In making public reports of quack remedies, it is usually advisable to omit the name of the proponent, because the very announcement has the effect of advertisement. One needs a delicate balance between notification and identification to effect the action desired.

At the national level, in addition to the Bureau of Investigation of the American Medical Association, there is the Food and Drug Administration, the National Cancer Institute and a Committee on Unproved Methods of the American Cancer Society. These bodies all help in various ways to investigate and report on differing phases of this repetitive problem; the F.D.A. aids in prosecuting certain offenders.

The Clinical Trial

The matter of adequate clinical trials in cancer therapy is carefully reviewed by Easson in a recent publication. "The clinical trial is a carefully and ethically designed experiment with the aim of answering some precisely framed question." It presupposes agreement on basic principles as to number of patients needed, type of patient needed, and type of treatment proposed. Ethical considerations are of the utmost importance. The group forming the two sides of a random trial must be so designed that in the light of existing knowledge either treatment is equally likely to be in the patient's best interests. Easson describes some clinical trials of the value of ovarian radiation in breast cancer (they showed that it does confer real benefit in terms of longer survival), and the value of parametrial irradiation in *localized* cervix cancer (it does not confer additional benefit to that obtained by proper radium therapy). He then goes on to write "Perhaps the greatest dogma in recent years in radiotherapeutic circles is concerned with the wonders of megavoltage therapy. It is curious how uncritical enthusiastic medical men can become when presented with a new instrument, a new drug, or even a new idea. Insulin, liver therapy, penicillin and cortisone were indeed epoch-making discoveries, but after the first enthusiasm a slow painstaking reappraisal was essential. This is over-due with megavoltage therapy. In Manchester several clinical trials have been initiated during the past seven years to try to evaluate megavoltage therapy using the 4 million volt linear accelerator. None of these trials has yet reached sufficient maturity for publication, but it is already clear that though morbidity from 4 Mv X-rays *may* well be less than that associated with kilo-voltage therapy, *there is no improvement in survival of the cancer patients treated.* This has been tested in patients with cancer of the *cervix* and cancer of the *bladder,* and the detailed discussion of this work will be published in due course."

Some Current "Remedies"

The following current unproved or unorthodox cancer treatments will be briefly illustrated with slides: (1) the Hoxsey treatment, (2) Koch treatment, (3) Krebiozen, (4) Lincoln (Bacteriophage), (5) Spears, (6) Savannah.

Selected examples of the following will also be shown: Adrenal cortex extract, Arginase, Electronic Medical Foundation, Gregomycin, Hett (cancer serum), Institute of Applied Biology, Laetriles, Mucorhicin, Rife-Ray.

Summary

History is veined with cancer charlatanism. Unorthodox and unproven methods of cancer therapy are still in extensive use today. The background of such therapy is one of unawareness or fear on the part of the patient, and ignorance or avarice on the part of the "healer." Its ultimate control is a problem of mass information — that many types of localized cancer are curable, and that medical research offers hope for other types.

Wider understanding of the immediate situation by medical educators should lead to better instruction of physicians and some reduction in the extent of charlatanism.

It is believed that regional or state cancer commissions should attempt to maintain facilities for making investigations of locally developing cancer treatment methods of an unorthodox nature.

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The Functional Approach

It is with the symptoms of disease that the patient, and that the doctor mainly, contends; and the symptoms of heart disease may be said to derive almost exclusively from faults in function. Therefore, in managing our patients, our thoughts must be chiefly set in terms of function and not of structure. To whom I fail to teach this first simple, but essential, lesson I have naught to teach.—SIR THOMAS LEWIS. *Diseases of the Heart.* New York, The Macmillan Company, 1933, p. vii.

Nutritional Quackery

Jean Mayer, Ph.D., D.Sc.

■ There is no true estimate of how much nutritional quackery costs the American people in terms of money. At various times, the American Medical Association has tried to make such estimates; these have varied between half a billion dollars to a billion or more dollars. Certainly, in many ways, the cost of nutritional quackery goes further than money alone. When the confidence of the American people in their food supply, their physicians and their universities is systematically undermined, the cost is very high indeed. When garlic pills are sold for treatment of high blood pressure or grapes for cancer, the cost is likely to be higher still.

The first step of nutritional quackery, this undermining of confidence in our foods is often not recognized. For nutritional quacks to be successful, they have to convince the public that the foods they buy in super-markets and eat are poisoned by preservatives and insecticides, and that besides, they were "devitalized" in the first place by the use of "chemical" rather than "natural" fertilizers. The medical profession and the universities are alleged to be in league with the food manufacturers in the exploitation of the public. The only remedy is the consumption of foods which have not been exposed to such nefarious influences. This is why even such apparently innocuous institutions as "nature" food shops or "health" food shops are dangerous. First, they drain a great deal of money that ought to go to normal food channels and medical care. This is particularly true for the older part of our population, which is generally speaking, less educated and poorer, and thus more vulnerable and in fact, more hurt. Secondly, the very existence of this business is based on distrust of ordinary medicine and thus naturally leads the consumer to the ultimate step—medical quackery. At least in our part of the country, there is a frequent connection between the promoters of health foods and nature foods and the anti-flouridationist movement; the more one delves into the problem, the more one tends to see that the special food or food supplement business is not just a matter of a harmless old lady selling blackstrap molasses to another harmless old lady, but a vicious and potentially dangerous national racket. Many such supplements are sold door to door as part of daily "family" programs. These supplements are usually advertised in the mail in very careful fashion because of federal penalities if they do otherwise. The door to door salesman, under no such restraint, will promise prevention or cure of dandruff, heart disease, cancer, gout, arthritis and make great capital out of what such products are going to do to retard senility, or cause rejuvenation of sexual functions. A statement from the National Better Business Bureau this last November mentioned that there were in excess of 75,000 distributors of Nutri-Bio in this country at present. This, for those of you who don't know it, is a program which will protect you against all the deficiencies you don't have by making you consume regularly pills containing an arbitrary amount of vitamins, as well as concentrates of such "natural" products as alfalfa. The sales talk can be obviously checked on in only the most cursory fashion. It is my understanding that The Food and Drug Administration has only six or eight individuals whose function it is to check on all such door to door sales. Those of you who are interested in finance, will like to know that on October 17, 1961, the Nutri-Bio Corporation filed a preliminary prospectus with the Securities and Exchange Commission concerning the offering of common stock held by six officers and directors. According to testimony given by Dr. Fredrick J. Stare, Chairman of the Department of Nutrition at the Harvard School of Public Health, before Congressman John Fogarty's Subcommittee on Appropriations on March 6, 1962, the prospectus "indicated that the gross income rose from $1,795,638 to $8,208,902 during the year ended July 31, 1961." It also indicated that Mr. Bob Cummings, the well known and pleasant television comedian, is a senior Vice President in Charge of "Nutritional Research." Again according to the prospectus cited by Dr. Stare in his testimony, "Mr. Cummings is a Director of the Corporation and its second largest stockholder (16 per cent). According to the aforementioned prospectus, his remuneration during the fiscal year ended July 31, 1961 was $74,641 plus $7,453 set aside under the company's profit sharing plan. The company also employs Mrs. Robert Cummings at a current salary of $3,333 per month with the understanding that the salary will be reduced to $2,000 per mouth when the Registration statement becomes effective. During the fiscal year ended July 31, 1961, Mrs. Cummings was paid $76,141. Each of the five Cummings children re-

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ceives $166.00 per month pursuant to a license agreement authorizing the use of their names by the company."

Companies similar to Nutrio-Bio usually originate in Southern California or Florida and then work their way east and north respectively. Another fad, this one originating from Florida, which has hit Massachusetts, is sea water. Sea water, somebody has discovered, is a source of minerals. It obviously is; the minerals are those found in food in general. All sorts of marvelous claims are made from sea water. It probably won't be long before some enterprising people start dehydrating sea water to produce a powder to which water can be added to make instant sea water.

It is rather amusing in this connection to note that sea water is a rich source of fluorine; and yet the same people who sell sea water are also the most adamant proponents of the idea that fluorine is a deadly poison.

Another aspect of nutritional quackery, and one which could be corrected by administrative action and education, is the nutritional quackery which goes with athletics. There isn't a fad diet in the country and there isn't a quack preparation which is not advocated somewhere by a coach or athletic director to the boys or girls under his care. Yet coaches are anxious to do well; but they have an extraordinary need for proper information They have great influence on the youngsters under their charge, much more influence than anybody who hasn't looked into the problem realizes. Athletic feeding in this country is in the dark ages. It usually proceeds on the assumption that enormous amounts of protein are necessary for athletes, a fact which has never been demonstrated and actually has been disproved. Furthermore, what passes for a high protein diet in athletic programs is usually extremely high in fat and, in particular, in saturated fat—meat, eggs, milk becomes the staples. In addition, all sorts of odd concoctions are fed to the boys and girls.

At one college I know, royal jelly became a daily item at training tables. At another college wheat germ oil has acquired quasi-magic properties. All sorts of very curious practices go on in weight control in athletics much as crash diets (with dehydration) before boxing events.

This is an area that ought to be given a great deal of attention. If coaches and athletic directors were well-briefed in principles of good nutrition, they could be very effective in reaching a great many adolescents who are almost impossible to reach in any other way.

Another aspect of nutritional quackery that all of you are familiar with, of course, is the subject of obesity. This is one I am particularly interested in because my laboratory and our department at the Harvard School of Public Health generally have been particularly concerned with the regulation of food intake, different types of obesity, treatment of obesity, and so on. There, I don't need to tell you, hardly a week passes by without somebody coming up with a miraculous diet or a miraculous drug, none of which, at present, have been shown to have any lasting merit. There are as yet no proprietary drugs sold over the counter which are really effective and safe to treat obesity. The drugs we have at present, either have no effect or if they have any effect, have a usually quite transient one. There is an accustomization of the body to these drugs, the dose then has to be increased, and by then the side effects of the drugs make them undesirable. Yet every day some modification of this or that previously known (and poor) drug is being placed on the market. I was recently asked by the Food and Drug Administration to appear as a government witness to try to get one of these preparations off the market, and was appalled at the price and time that was involved: two full days on my part, two days of a professor of Pharmacology at Johns Hopkins University, two or three days of a professor at the University of Texas, several days by distinguished clinicians and of course a great deal of time on the part of a busy Federal judge. All this is not to say that for certain patients, and under proper medical supervision, there is not a good case for the use of such powerful agents such as amphetamine. But there is no place in therapy for self administered medication on the base of a fancy label.

Nutritional remedies for arthritis are another of the favorite hunting fields of the nutritional quacks; and this illustrates another situation, which not infrequently leads to nutritional quackery. Whenever people lose hope of getting cured from medical treatment—because there is no known cure —they listen to quacks. A study of a large population of arthritis patients revealed that half of them have gone to quacks at various times and have followed faddist dietary treatments.

Old age patients are frequent victims of nutritional quacks. I've alluded to this already. Older people are poor; they are often less educated. They do have one special nutritional problem, and only one which is directly a result of old age, and that is that they often lack teeth. One of the reasons why nutritionists are interested in fluoridation is not merely because children are going to have less dental cavities, but because the benefits of fluoridation are lasting, and eventually older people are going to have teeth if their water was fluoridated when they were young. The lack of teeth in the aged tends to make them eat, very often, fewer and fewer foods because of the difficulties of chewing; and when those foods are those prescribed by nutritional quacks, odd and expensive items, then the risks of malnutrition are very much greater.

Let us now review the main methods by which nutritional quacks misinform the public. We have already mentioned in another connection, the special shops which are very often centers of distribution of quack literature, as well as not infrequently of anti-fluoridationist propaganda.

In some cases, of course, "nature foods" are outright and complete frauds. For instance, the Food and Drug Administration has discovered in Boston a little "factory" where labels of cans, usually cans you would buy in super-markets, were simply ripped off and a new label substituted, assuring the public that the food had been grown without insecticide and without chemical fertilizer, and the price was hiked up accordingly. Raisins which were sold in Boston and supposedly had been grown without insecticides or fertilizers were followed all the way to the vineyard in which they had been grown in California. The farmer there had absolutely no idea that this was the eventual destination of his grapes, which he was growing according to the customary methods including insecticides and fertilizers.

Door to door salesmanship of a nutritional preparation is extremely prevalent and dangerous in that this is often where the most dangerous misinformation is given, away, supposedly, from the dangers of being overheard or read by federal or state inspectors. Very often the salespeople are innocent individuals who were recruited from the community and told that this was a nice and useful way to increase their income; they would be doing their neighbors a favor by selling them Brand "X" program which would save them from various diseases.

Books promoting fad diets or foods are a more and more common threat. Our Department compiled a list of the books we would like everybody *not* to buy because we think they misinform the public on the field of nutrition, and I will cite some of the titles: Arthritis and Common Sense by Dan J. Alexander; Folk Medicine, A Vermont Doctor's Guide to Good Health by D. C. Jarvis and the Jenry Holt Company. This was one of the most popular books for a long period—remember, that's the honey and vinegar treatment; Feel Like a Million by Catherine Elwood; Health Through Nutrition by Leaonard Cordell; Let's Eat Right to Keep Fit by Dell Davis; Look Younger—Live Longer, by Gaylord Hauser; Life Through Juices by H. E. Kirschner, M.D.; Live to Be 180 by Justin Glass; Calorie Count-Down by Victor Linglar; The Poison in Your Food, by William Longgood; Stay Young Longer by Linda Clark; Eat Your Way to Better Health by Andrew Rosenberger; and finally, Calories Don't Count by Herman Taller, M.D., Simon and Schuster, 1961.

"Health" lecturers are one of the sources of misinformation for the public, either through public lectures or through the radio, a medium which after all, is licensed by the federal government. The Food and Drug Administration has tried recently to get some of the better known quack nutritional lecturers off the air, but so far with indifferent success. Magazines and newspapers have difficulty in resisting the lure of advertising profits. Only responsible editorial polices are what stand between an informed and a misinformed public and, by and large, we don't have that in the field of nutritional advertising.

What can we do about all this? The first thing we need is a resolve among ourselves not to stand idly by while this fad information is given to the public. And first we should enroll our professional organizations. To name but one, the American Medical Association has been lax and lacking in the moral indignation that it can summon on other subjects when some of its own members have been among our chief offenders. We have got to summon the courage to speak up against nutritional quackery even if it does mean that we are going to get a great deal of personal abuse and occasional law suits. We must explore the avenues of informing the public, and I think that the schools are one place in which it can be done, not by adding one more small program to an already confused curriculum, but by insisting that all high school children go through at least one course—a good course—in human biology and physiology as part of their general culture. This course can be used to dispel the misleading information that they are subjected to. And, again, I would suggest that coaches and athletic directors are natural allies of ours in health campaigns.

We need to give much more support to the Food and Drug Administration, and in many states, to the local Food and Drug Administrations. Those agencies simply don't begin to have the personnel and the authority they need to do the job they would like to do. Finally, we need to take and use the same media as have been used by many of the nutritional quacks to give good solid nutritional information. We must cultivate our relationship with the newspapers, with the radio, with television, be of help to them so as to be on the sort of terms which enable us to put some personal pressure whenever needed to get off the air the most noxious type of programs or by contrast, to bring on the air the sort of programs that need to be done. There is a certain reluctance among the medical profession and among academic people to do this, and yet it is essential. Somebody is going to advise the public on its diet and it might as well be the people who know something of what they are talking about.

Quackery And The Consumer

Responsibility Of The Medical Profession

Irving Ladimer, S.J.D.

I wish to discuss not so much the effect of quackery on the consumer but the responsibility of the professional person who provides data, scientific and otherwise, which may eventuate in some form as advertisements to the general public. I have therefore subtitled this paper "Responsibility of the Medical Profession." In other words, I am going to the origin of many of the presentations which reach us as consumers and potential consumers, because I believe that rigorous self-discipline at this stage and an appreciation of the scientific, ethical and even legal implications by men of medicine may help considerably in preventing the deception, distortion, and just plain confusion which confront the public every day in promotions of certain health products and programs.

The Better Business Philosophy

I should like to start with some explanations, some history and definitions.

First, let me describe the purpose and function of the Better Business Bureau movement in the United States, which has provided a half century of service. We now have a network consisting of The National Bureau and well over 100 local Bureaus in major cities, united through the Association of Better Business Bureaus

The cornerstone of the Better Business Bureau structure, which had its origin in vigilance committees to detect and eliminate improper business activity, is self-regulation. This method can help control abuse while advertising is planned or proposed, thus preventing possible harm to the public and to competition. The most effective work, therefore, is often done before the claim is exposed. The Better Business Bureaus are independent, nonprofit organizations, established and maintained by business firms, including media, to protect themselves and the public from selling practices and advertising which are unfair, misleading or fraudulent. All reasonable means are used to discourage practices which impair honest and effective seller-buyer relationships. This philosophy of enlightened self-interest rests on the willingness of business to discipline itself and to employ professional support in the public interest.

The Bureaus are in the unique and fortunate position of not having to charge for their services. Any responsible question is given fair consideration and a responsible answer, based on information that may be made public with respect to a business firm, its products, services, and method of operation. In effect, this function of inquiry and review has been delegated to the Bureaus by industry and the public, as a systematic and efficient service for all. The Bureaus seek voluntary cooperation; they are in no sense law-enforcement agencies, nor do they hold any official standing as a governmental unit at any level. Their prestige and influence are based on the completeness, fairness and accuracy of the data provided and the logic in their analysis of the facts obtained from authoritative sources.

There is a basic difference between Bureau procedures and those of government agencies which include enforcement of laws prohibiting false, deceptive or fraudulent advertising and supervision of labeling of food, drugs, devices and cosmetics. As an agency premised on voluntary self-regulation, we hold that the advertiser should prove his claims before making them. Government, on the other hand, must assume the burden of legally proving that the advertising is false, misleading or otherwise contrary to statute. It is, therefore, in many respects held to a narrower field of activity. Bureau activity considers business performance, consumer effect and ethical propriety, as well as legal sufficiency.

The National Better Business Bureau is the agency for nationwide or regional business and shares its information with local Bureaus. In 1961, 100,000 requests for information were answered, of which 7,000 came from advertising media—newspapers, magazines, broadcasting units for the most part. I am constrained, if not necessarily pleased, to say that requests relating to drug and cosmetic advertising were among the most frequent.

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The Food, Drug and Cosmetic Division of the N.B.B.B. is mainly concerned with advertising of services, processes, products and devices in the health areas. Here, false, fraudulent and highly exaggerated claims may result in inappropriate self-treatment with worthless products. Misrepresentation may lead to delays in obtaining necessary and competent medical treatment, causing injury to health as well as to the pocketbook. Although this Division does not maintain its own laboratories or other facilities for testing, it is served by a panel of medical consultants who render opinions without charge (and even without the benefit of citation). We also enjoy the cooperation of organized medicine, professional societies and voluntary health organizations.

We do not enter into the doctor-patient relationship or, for that matter, into professional relationships. We are self-limited to representations which affect the public directly, although we also see the professional as a member of the public. Although this Division appreciates the role of the physician, it also recognizes—as does the medical profession—the place of self-medication. Our basic role is to protect the public against deceptive advertising of proprietaries.

Quack, Quack

To create and maintain an honest, open market, certain excesses of advertising which accompanied the vigorous, bold and even reckless growth of American enterprise had to be curbed. Not surprisingly, the first and most compelling outcries were leveled against the sharp and conniving and, regrettably, successful minority of health hucksters who "took" the public for worthless pills, elixirs, secret formulas and pseudo-scientific claptrap of all kinds. American quackery dates back, at least in legal recognition, to 1630 when Nicholas Knopp of Massachusetts Bay was punished for vending as a cure for scurvy "a water of no worth or value . . . sold at a very dear rate." This was done relatively quietly, before the era of exaggeration by broadside and pamphlet, the flamboyant newspaper ad and the deceptive package.

Many of you are doubtless familiar with the Tractorean or Perkinean rage that swept our country at the turn of the 19th century. James Harvey Young in "The Toadstool Millionaires"[1] a social history of patent medicines before Federal regulation, describes the promotions of Elisha Perkins and his son, Benjamin, who gulled patient and physician alike, with the marvels of so-called tractors, a pair of three-inch metal rods adroitly applied, one colored gold, the other silver. These allegedly drew out the noxious electric fluid, effecting cures in every limb and quarter. Perkins was initially successful in enlisting business, the clergy, medical professors and doctors, particularly the Connecticut Medical Society to whom he first announced his hardwares. He was actually invited, although not a physician, to address the Society in 1796.

In all fairness to your Society, let it be said that they reconsidered during the year, and instead condemned the "miserable remains of animal magnetism" and resolved to expel any member using them. Young comments, "it has been suggested that certain stalwart physicians in the Connecticut Medical Society and some members of the faculty at Yale were greatly shocked by the galvanizing trumpery that had arisen in their midst. From this sense of outrage, at least in part, was to come the founding of the Yale Medical School. This unintended result may be viewed as the most lasting legacy of Dr. Perkins' metallic tractors."[1]

Before we laugh too unrestrainedly at the absurdity of such notions and the gullibility of *homo* more or less *sapiens,* recall that any diversion from the wretched purgatives, cathartics and other violent medicine practiced by the recognized profession at the time would have been welcome. And Benjamin Rush's influence for strong physik and for bleeding, even though questioned, still held such an authoritative command on the profession that common sense and experience could not upset it.

And lest we too quickly sigh and say this is over, may I remind you that only months ago the FDA seized a quantity of so-called electronic machines, titled "Micro-dynameters." These machines, like their less complicated but equally promising ancestors were reputed to be able to diagnose practically anything. The sober description of the FDA suggests that at best they measured perspiration by simple string galvanometry—at $600 to $875 a piece. I presume the payments were sweated out of the patient.

These are scandalous but, in administrative operation, simple matters, since the fraud is apparent at once and instant exposure indicated. A recent book on bee venom as a cure for arthritis, the conflicting claims in the name of cholesterol and safflower, the offhand or apparent acceptance of shot gun vitamin-mineral compounds and food supplements, the host of alleged energizers, vitalizers and pep pills and their opposite numbers among so-called sedatives, tranquilizers and relaxants (all non-habit forming, of course) present far graver problems especially to those of us who must depend on scientific medical reports of a specific nature before rendering an opinion which may in effect kill or sell pills, powders, pastes and other preparations.

To my knowledge, there is no single definition of quackery. A dictionary may explain it as practice by one who is not qualified, that is a pretender to medical skill or experience, who for questionable or improper motives promotes remedies and cures for diseases and for other conditions which he knows or should know cannot be helped by what he has to offer. Such fraud implies knowledge and dishonest intent, but in fact the effect on the consumer is the same whether the perpetration is willful and knowing or inadvertent and careless. As Miss Russ, my predecessor, rightly asked "Do consumers care whether something is not technically a fraud within the narrow confines of the law if they have been deceived into purchasing a product because of false or misleading advertising claims?"[2]

Experts report that today medical quackery is a billion-dollar racket, operated by educated, sophisticated men, adept at jumping through legal loopholes and gaining specious support for medical claims. The captivating chronicle, "The Nuts Among The Berries" says that over a half a billion dollars goes for food remedies and 350 million for needless vitamins and over 100 million more for weight-reduction schemes and products.[3]

Why Quackery?

I see three major problems or areas with which we ought to deal.

First, there are the schemes to make money, grafting on the gullibility of the public. Here we have outright pickpockets who use indirection to reach the savings of our people. These unscrupulous dealers have no purpose other than to take what they can, preferably as quickly as they can. The only condition they seek to relieve is an overweight bankroll.

A recent example of an advertising deception in 1961 exposed by the Bureau was the sale of concentrated sea water, allegedly helpful to persons suffering from arthritis, cancer, diabetes, and other illnesses. The Bureau's bulletin helped to stop advertising and, therefore, to stop sales. The Food and Drug Administration proceeded to seize a number of the sea water preparations based on false labeling. Add to this the food fads which attribute properties of health and vigor to kelp, parsley, wheat germ, molasses and the host of so-called natural products. Add also the devices for weight reducing such as plastic garments, exercisers, vibrators and the accompanying laxative, dehydration drugs and alleged appetite depressants. The vast majority of the public as well as organizations such as those represented here recognize that such utterly useless materials touted as aids should not be sold or purchased, but there are still many who fall for the fakeries—and these are entitled to protection given only by truth.

Far more difficult is the second area of concern. These are proposals, honestly or evidently honestly proposed, to relieve serious conditions of nutrition, arthritic disease, forms of cancer, nervous disorder and perhaps to improve or sustain various sensory conditions such as seeing and hearing. Frequently, questionable and perhaps injurious regimes with or without specific products cannot be properly distinguished and reasonably differentiated from potentially valuable treatment and honest research. Legitimate investigation, as we all know, often has its origin in a struggle among a variety of possibilities to arrive at a right solution. Sometimes, a solution is not found, but the concept cannot thereby be condemned. These theories and ideas are offered not infrequently by physicians of high standing and repute and by organizations sincerely attempting to help, but also, unfortunately, by others who see a good thing in trading on the misery and the pain of countless individuals who suffer from disease, or who think they suffer from disease. None of us wants to impede or obstruct medical progress by dampening the possibilities of honest research and experimentation. Medicine and science generally, although basically future-oriented, has not always been kind to innovation.[4]

We must try to keep the line between that which science offers today as possible and probable and that which is not. Speaking from my years of interest and experience in the field of human experimentation, I am the first to say that I consider it, if not unlawful, certainly unethical to use the human being first as unknowing subject or as an unwitting patient in a doctor's office. Of course, he may validly volunteer to participate in an organized clinical test or investigation.[5] We must be extremely careful to be sure before we pontificate that there is no basis for a claim. We are all too familiar with the instances of attempts considered wrong or stupid, later realized as right and appropriate. The need to advance knowledge through research on untried drugs and procedures and to practice proper conservatism in the care of patients presents medicine and, in turn, all of us with this difficult dilemma.

Third, we are confronted with problems of a different order. This is a field bordering medicine, but which medicine is forced to enter. I refer to the variety of products and notions and methods and schemes which relate to appearance, social acceptability and perhaps even economic potential. The quests for beauty, virility, sexual attractiveness are not solely vanity problems to be dismissed by scoffing at the puffing of cosmetic advertisers. In our society, these needs are equally significant. A recent French government ruling includes lipstick as an essential in determining living costs. And, in our country, we have long recognized the deep importance of cosmetic treatment and surgery. They go deeply to the goals and values of our way of life which literally demands these attributes for marriage, raising a family, holding a job, making friends, and demonstrating an interest in the world around us.

It was always thus, I am told. But with greater freedom today and less demand on our time and energy solely to survive, this concern is elevated to an almost frenetic and constant pursuit. Not infrequently, this pursuit leads to significant health hazards. The squeeze to a sylph-like figure often thins into malnutrition. Our intense desire to look healthy and tan may yield to overexposure, possibly the beginnings of skin cancer. Insistence on health foods and diets may tear us down, rather than build us up. Our attempts to get hair when we don't have it and to remove it when we do not only may relieve us of the pence in our pockets but of whatever good looks we may have. The loss is, therefore, not only time and money but health, physical and emotional. There may be a considerable invasion of the inner security and peace that we today so significantly need.

In summary, we may regard quackery in the health area in its broadest sense as a social phenomenon employing questionable or disputable claims as a method of selling to the public. A campaign against quackery, so defined, is best prepared by understanding the bases or origins of such phenomena. From my analysis, they would appear to spring from obvious frauds, perpetrated to push a product by evading or shading the truth. Second, there is the promotion not substantiated by science in theory or performance, but likewise not disproved, and therefore subject to question. Third, there is the appeal to beauty, well-being and social grace which on surface appears no more than reasonable self-gratification but which may impair physical and emotional health.

The Care And Nurture Of The Quack

Why is it then, despite a more sophisticated consumer, a more alert profession, a host of Federal and State agencies regulating advertising, labeling and communication and a stronger structure of self-regulation, that deception and bilking of the public continues? Most of the crude and tawdry forms of advertising have disappeared and the circus-type of appeal has given way to references to medical endorsement. But, the fundamental come-on, although more subtle, still enchants, captivates and ultimately ensnares.

There are several explanations:

First and foremost, of course, is the average consumer's pitiable lack of scientific knowledge in most matters pertaining to health. Add to this a general inability to accept the fact that there are certain diseases for which no cure is yet known to medical science; the perpetual search for the "fountain of youth" which seems to permeate our society; the eagerness of the afflicted to believe promises of the quick, easy, "miracle" remedy; the naive belief that if something is printed "it must be true!"; that advertising claims must be true or media would not permit them, or the government would prohibit them; the fact that some media assume little responsibility for protecting their audiences from fraud by questioning copy claims. And we have a climate in which false, deceptive or fraudulent promotions flourish.[2]

Secondly, there is the problem of prompt and effective enforcement of the federal laws which prohibit false, deceptive, or fraudulent advertising and labeling of foods, drugs, devices and cosmetics. Responsibility is divided among three agencies. The Post Office Department is empowered to bar use of the mails to those who seek to obtain money through the mail for fraudulently advertised products. The Food and Drug Administration acts against false or misleading labeling of foods, drugs, devices and cosmetics. The Federal Trade Commission has primary responsibility for the regulation of false and misleading advertising (other than labeling, although advertising materials may sometimes be used in such a manner as to become labeling).

In addition to the difficulties of proof of statutory violation and divided jurisdiction not only among Federal agencies but national and local agencies as well, there are open areas where no government agency has clear power, such as expressions of opinion (as in the case of faith healers and health books) not associated with product promotion, and the frustration of time. It is not only the simple factor of time to investigate, notify, prosecute, adjudge and establish compliance, running into months and years, but the ingenuity of firms in obtaining legal delays and in effecting changes in business operations. And during this period, an entrepreneur may sweep the country with the challenged advertising through direct mail appeals or media willing to accept it.

Commissioner Larrick of the FDA concedes that we may have oversold the country on the extent and effectiveness of government control. The new powers to be assumed by the FDA, in the period which may well become known as A.T. (after thalidomide), may tend to strengthen the public conviction that everything on the market must somehow be O.K.—if not approved, at least not dangerous. They do not realize that the laws extend to fairly limited areas. Even the advertiser who has been rebuked or ordered to cease and desist may feel he is in the clear as long as he is not tailed by a Federal officer. There will never be sufficiently large staff to watch each dereliction, so we cannot wholly substitute—even if we choose to—government policing for consumer vigilance and self-regulation.

Finally, as Dr. Herbert Ratner has reported "America is the most over-medicated, most over-operated, and most over-inoculated country in the world. It is also the most anxiety-ridden country with regard to health."[6] "We make health an end in itself," not simply a means to do our work and to enjoy living. Assuming the truth of this charge, it is obvious that every new (and we certainly are addicted to the new) medical messiah will quickly recruit disciples and converts. Eager converts are as likely to be as uncritical in their acceptance as the persuaders are in their promises.

Professional Awareness

I have recited these problems and restated some of the reasons for the current situation not because you are unaware of them but because, as guardians of the public trust, professionals have a responsibility at least for cutting such troubles down to manageable proportions.

In the health field, it is not easy to determine what is based on scientific proof or to evaluate what is proffered as such. Although we proceed by asking the advertiser to submit supporting evidence, we do not immediately write a critical report if we get no response or one lacking substance, but try independently to arrive at the facts. We are frankly more pleased to find a basis for honest sale and to provide suggestions for fair copy than to have to negotiate to a stalemate or rejection. We, therefore, must turn largely to the medical profession for help in this respect. We look to you to provide data, to help evaluate what is submitted and to suggest further inquiry.

The Troubles With Doctors

Since the medical profession, as individual physicians and through its academic and scientific societies, has generally requested the right to express views on the worth, efficacy, safety and proper use of diagnostic and treatment modalities, we, like others, have referred our problems to them. We are pleased to do so. We know that advertisers are leaning toward such support, rather than the testimony of baseball players, and actors and housewives in order to convince the public.

It is, therefore, appropriate to outline some of the difficulties or experiences we have had in trying to ascertain that which can be considered scientifically supported.

THE "SCIENTIFIC" PAPER

To get at the basis of a claim, we look for the results of a clinical test, preferably as reported and published in a recognized scientific journal, either furnished to us or otherwise obtained. We are frequently astounded to find that reports of clinical tests in scientific journals turn out to be little more than abbreviated opinions signed by an M.D. A paper submitted described in three sentences, without any other data, the alleged results of an examination of a sample of twenty patients before and after use of a health device, concluding "all but one stated he was improved." It may well be that such an opinion represents a summary of extensive work, properly controlled, but how can we be certain? And how can we be certain that absence of a comment on proper use, side-effects or qualifications constitutes assurance that there is no problem? A good study deserves a good paper in a reputable medium. The profession expects this and so do we.

THE "PROFESSIONAL" INVESTIGATOR

Then there is the professional investigator. I refer here not to the honorable scientist, requested to render an expert opinion, but to the "professional" apparently always available for a study which someone wants him to do, whether or not he is qualified. I do not add "at a price" because I know that some evidently are interested in fame (such as it is) not fortune. As in my field of law, or in any other profession, it is practically impossible for one person to be able to do everything. Even if he is familiar with scientific method, he is just not able to cover the large variety of subject matter, techniques and other necessaries required in performing adequate scientific studies. Yet, we have noted names which occur repeatedly and with increasing frequency on papers which are claimed to be independent studies. Sometimes these men are hired as consultants directly by drug or other firms, sometimes through so-called independent research or testing laboratories or they advertise themselves, contrary to ethical standards. This is of little consequence. The ubiquitous eminent physician should be questioned even if qualified, simply because we cannot conceivably be all and always, yet care for patients or conduct serious longterm studies.

One physician advertised for more than thirty years as a medical consultant in all fields. This character was described in some detail at the National Congress on Medical Quackery about a year ago. In some ads, he claimed to have just the evidence needed to support drug claims based on a survey of American or foreign literature. He also offers services in handling labeling, writing articles or brochures and ads with professional appeal. His advertising has included products available under "exclusive license" ranging from soporifics, arthritic drugs, reducing aids, athlete's foot remedies to hay fever cures and ulcer remedies. He has operated as a member of a team with other physicians who pass around the clinical testing much as a medicine ball is tossed around a circle.

THE "HOUSE" DOCTOR

After repeatedly requesting clinical data in support of a claim for a new feminine hygiene product, NBBB finally received a set of papers and references, all cited to local medical journals. The investigations were all conducted by men who had been granted stock options in the manufacturing house. Another instance involved the president of a sea water concern who was a physician and endorsed the claims.

Although this company doctor may be honest and straightforward, is it possible to be free from influence and, if free, to convince others? As a physician, he is both vulnerable and suspect. While doctors, like others, may invest in or even control business firms, their ability to render objective scientific reports on leading products of the firm is so diminished that they devalue themselves and the products they endorse.

RIGGED RESEARCH

Dr. Kenneth Milstead, Deputy Director of the FDA'c Bureau of Enforcement, calls attention to an area of quackery which he terms "repulsive and abhorrent to all scientists." He cites two problems: (1) "tailored studies," which generally consists of a few uncontrolled observations on a few patients, later described by the advertiser as "clinically tested" or scientifically supported; and (2) predetermined results, wherein the physician does not actually test, or fixes his tests to come up with the desired answer. These are, according to Milstead, the ultimate in quackery, representing man's worst meanness to his fellow man.[7]

INCOMPETENT RESEARCH

Almost as reprehensible as the tailored trial or the cooked-up clinical study is the outright incompetent or inadequate study. The medical man who conducts poorly designed research, or employs faulty design or selects a biased sample or fails to account for side-effects, qualifications, lost cases or exceptions, or who misuses statistics and, finally, who draws questionable conclusions from data may be honest but is just as blameworthy as the scientist scoundrel.

A Canadian researcher assessed the methods and techniques of 103 studies published in the Canadian Medical Association Journal and the Canadian Journal of Public Health.[8] He found that in 17.5 per cent of the articles, terms or systems of classifications were not explicit; in 90 per cent, sampling was inadequate or inapplicable; as to controls, 35 per cent had none, 13 per cent were inadequate, 25 per cent were well controlled and 27 per cent were studies where controls were inapplicable; in respect to statistics and their use, over 57 per cent used inappropriate methods or required additional analysis; and, finally, in the derivation of conclusions, 42 per cent of the articles contained flaws of inference, particularly in assigning causal relationships.

While these articles represent the sins of our neighbors, I doubt that we Americans can cast stones. It is likely that our published scientific reports suffer to a similar degree. At the NBBB, we have had to write for explanations of differences between samples originally selected and those reported; of omission of controls; of use of averages rather than distributions where the spread was evidently significant; for bases of conclusions on ridiculously small universes and for rationales supporting alleged cause-effect propositions. These are technical problems, not necessarily misunderstandings of scientific method. But I was astounded to find that some advertisers (and perhaps their medical consultants) apparently honestly argued that trials of one drug could apply to another which they specifically said was different; that results achieved by a high-powered air purifier could be ascribed to a smaller, less powerful model; that the known properties of one ingredient could be attributed to a mixture or compound without further test; and that increased efficacy or "power" would naturally follow in all cases from increased dosage in a straightline relationship.

JOURNAL RESPONSIBILITY

That such papers are published gives one pause. Medical journals, held out to the hallmark of "research," regrettably become inadvertent co-promoters of quackery, when they permit their pages to be filled with questionable or spurious reports. Yet, these journals, either because of interest in advertising, reprint sales or perhaps sheer incompetance or lack of time on the part of editors, allow such things as: a paper comparing an alleged new over-the-counter item with a prescription drug, although no prescription drug was used in the tests; a paper signed by doctors who turned out to have no medical degree; a paper based on a test presumably prepared by the author but in fact done by another; a paper with references to a product claimed to be the same as that under study but in fact different; and numerous papers without identification of samples, method of selecting subjects and, of course, conclusions based on statistics not given or improperly computed.

I must conclude here that although not all journals are lax in screening, there are enough cases to warrant much closer scrutiny,

HEALTH BOOKS AND LECTURES

Reference to publications cannot be concluded without remarking on the spate of so-called health books and health lectures to the general public. Written by physicians as well as laymen, they can and do create as much havoc as specious specifics for any disease. Erwin DiCyan recently wrote of "tainted books" in this field, describing among others health fads and nature food volumes, dietary remedies such as vinegar or molasses for all kinds of disease, promotions of natural remedies such as candle wax, baking soda and water for all manner of ailments.[9]

Books employed as labels and held to be labeling for products are clearly subject to Federal statutes, as shown in the recent celebrated case of "Calories Don't Count" by Dr. Taller. But others, equally pernicious, may live on as expressions of free speech. Whether or not government agencies or bodies concerned with self-regulation such as NBBB can or should move against books as against products is an open issue, but it is clearly within the realm of the medical fraternity to criticize them vigorously and to stand as strong witness to professionals and to the ordinary reader against instances of misleading advice and information. The same holds true for the health lecturer and healer—who fogs the air with misty ideas and half-truths. Those who are in fact licensed physicians or dentists can be read out of the profession by the vigilant members and those who are not can be denounced in other ways. Dr. Lasagna comments that the effects of certain medical writings by or about doctors have already "seriously impaired patient-doctor relationships."[10]

CONSULTANTS FOR SALE

I wish to call attention also to the case of the medical consultant who does not fulfill his obligation to himself, his client and thus to the public who relies on both. Recently, we came across a brochure replete with reference to the work of a well-established nutritionist who, on inquiry, was found to be the paid consultant to the vitamin distributor. Both acknowledged the relationship, but the consultant evidently hadn't been consulted for months, although he had regularly cashed his check. He admitted that he had not seen the copy quoting him, was unaware that sales representatives were to be taught about his formulation and plainly "had not kept in touch" although he was, by contract, responsible for all scientific matters including advertising of claims. Likewise, the firm did not call on him or even indicate that copy had been developed. We trust this is not typical but we suspect that all too often a name is bought and the expertise is not. Responsibility rests on all parties to see to it that science is used, not abused.

Responsibility For Follow-Through

Finally, we reach one of the least discussed problems, but one of outstanding significance: that is, the responsibility of the reliable investigator who is honestly interested in making a serious contribution to see that the interpretation given to his work in advertising and in any other disclosure is accurate and is presented as intended. All too often, the carefully documented study of a reputable man finds itself in syncopated print with dots and dashes, or presented in extracts, far from the meaning of the basic and original context. These are not necessarily wrong; they may simply be inept, inappropriate, or unable to constitute an understandable whole.

It is my strong opinion that physicians and other scientists who recognize that their work may be quoted have the further responsibility of insisting and insuring that quotation and use is proper. It is true that many physicians who write for journals have no way of knowing who will pick up papers, who will use quotes and will cite references. On the other hand, it is also true (and this applies to a large majority of physicians when they are in fact testing a product or process under grant or contract) that many are in position legally, ethically, and professionally, to require that they have the right to check and clear before their papers or summaries are issued to the public. Perhaps this will impose a great burden. They will have to review how eager advertisers and copy writers and promoters use the medical word as the basis for the selling word. Nevertheless, unless they exert this responsibility, unless they recapture the right and power so many have surrendered, we will have to turn to them again and again for the basic research which should have been cleared in the first place. Our reliance, after all, must be based on experience. Those who now prepare clinical papers on products for the people should follow through so that the scientific expression retains integrity.

Effect On The Consumer

Before closing, I will confess that I asked myself whether these criticisms were warranted. Can't we rely on the consumer? It is said that if the consumer is consistently misled or swayed from side to side like a spectator at a tennis match by unscrupulous promotion and misrepresentation, if he is regularly defrauded, he will simply stop buying, except when he has to. We also like to believe that when good quality is placed alongside shoddy material, the choice will always be for the former. These statements unfortunately partake of as much hope as fact. This is not to say that I am cynical, but I really do not believe that quackery is self-defeating or that intelligent judgment will prevail.

I conclude rather that active, positive programs of self-regulation, professional responsibility and governmental control in proper proportion must be vigorously pursued in the public interest. Perhaps in time the lion will lie down with the lamb but right now the lamb needs the shelter of the shepherd and the fold.

Therefore, I would like to restate the general position of the National Better Business Bureau and my own as well: that self-regulation, self-control and discipline is the way in which business and the professions can reduce the fleecing of the public as well as avoid criticism and the likelihood of outside restraint. Self-regulation is not as invidious or difficult as it appears. For the medical profession, of course, the concept of a practical code of ethics is virtually as old as medicine itself. A further application of the code to protect and enhance the use of scientific studies for the general public should be a welcome addition and a proper duty. If we at the Bureau are expected, as partners with you, to protect the public from either the outright quacks and frauds or the well-intentioned practitioners, we should be able to look to you, the profession, for the right word, the honest word, the properly interpreted word. If this is not forthcoming, you will have far less occasion to blame what occurs on others. After all, when the mirror is turned, you are the others.

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Surgery And New Knowledge

Whenever a region of the body has been made accessible to surgery, a new insight into its pathology has resulted from the fresh experience that has been acquired of morbid processes in the living and especially of the earlier stages of disease. This has been abundantly shown in the case of the abdomen and the case of the thorax.—*The Collected Papers of Wilfred Trotter,* F.R.S. London, Oxford University Press, 1946, p. 48.

The Role Of The Post Office Department In Preventing Medical Quackery

Thomas Peckenham

■ You perhaps have heard the story about the English sailor who reported that he had cured his broken leg by treating it with tar and oakum. He was being truthful—but—he failed to mention that it was a wooden leg. An unscrupulous promoter could have obtained many letters testifying to this "cure" and could undoubtedly sell tons of tar and oakum to a gullible public. If the promoter carefully worded his advertisement, it is possible that he could escape prosecution. It is the gray area of advertising that often keeps the medical quackery promoter within the bounds of the written law—and incidentally makes him the bane of the postal inspector's existence.

The mail fraud statutes, Title 18 USC 1341, and Title 39 USC 4006 place a responsibility upon the Postmaster General to prevent the postal establishment from being used in the perpetration of schemes to defraud the public.

Investigation of medical fraud cases are conducted by a special group of inspectors who work directly from the bureau of the Chief Postal Inspector in Washington. They maintain liaison with the Food and Drug Administration, Federal Trade Commission, Department of Justice, and other governmental agencies

Although, postal inspectors still occasionally get old-fashioned medical quackery items involving electric belts, buzzers, bell-ringing machines, and even black magic potions guaranteed to cure all manner of disease, there is a new look today in such mail frauds. Promoters do not so often promise outright cures for serious diseases, but offer preparations to "aid" in curing various conditions which the American consumer finds undesirable. Probably the chief items in the category are the panaceas offered for weight reduction. Diet and weight control have become almost an obsession with the American public, and, perhaps, properly so; but it is unfortunate that people will risk many dollars on doubtful or dangerous preparations, where a visit to the family doctor would do the job more safely and effectively and in the long run probably more economically.

Government control over the health hucksters has been greatly strengthened in recent years; however, they are an ingenious lot and are constantly devising new methods by which they may continue to market quack remedies without interference. Notable examples of this are found among those who have gone south of the border to broadcast claims over Mexican radio stations which would not be permitted over domestic stations.

This problem came to our attention shortly after the meeting of the National Congress on Medical Quackery in October, 1961. Broadcasts from these stations are beamed across the border into the United States offering for sale misrepresented merchandise, including numerous medical preparations. Representatives of the postal inspection service met with representatives of the Federal Communications Commission and the Department of Justice. It was decided that the FCC would monitor such broadcasts and furnish tapes to postal inspectors, who would undertake investigations to determine whether the mail fraud statutes are being violated. This plan is now in operation and the Attorney General's office has alerted United States attorneys throughout the nation to the situation. We are pleased to report that the first 3 cases presented to the grand jury at Forth Worth, Texas, in January, 1962, resulted in the indictment and arrest of 4 promoters engaged in the sale through the mails of "Ease" and "Oceantone" for various ailments. Additional cases are under investigation and these will be presented to United States attorneys as soon as possible.

The indictment and arrest of Mrs. Cora Galenti Smith at Las Vegas, Nevada, in January, 1962, marks a further step in the drive against medical frauds. This self-styled beauty scientist attracted customers from all over the United States and as far away as South Africa and Australia, who were anxious to obtain her treatment, which would effect "glorious facial rejuvenation that completely erases 20, 30, and sometimes 40 years of sags and wrinkles." The treatment consists of peeling the skin through application of a cauterizing solution, allegedly car-

Delivered before The Connecticut State Congress on Medical Quackery, Berlin, Connecticut, September 26, 1962.

MR. THOMAS PECKENHAM, Postal Inspector, Hartford Post Office, Hartford.

bolic acid, postal inspectors located a number of women who had been victimized and in some cases disfigured by the treatment.

We are pleased to report that local medical societies affiliated with the AMA have been most cooperative in assisting our inspectors by providing us with the names of qualified doctors whose testimony is essential to the investigation and prosecution of these cases. Such assistance is sincerely appreciated.

In closing, we wish to assure you that our program against medical fraud is rolling and will be continued. It is our intention to give the public the maximum possible protection under the law.

Inertia vs. New Ideas

Apart from the happy few whose work has already great prestige or lies in fields that are being actively expanded at the moment, discoverers of new truths always find their ideas resisted. The consideration of this process is often obscured by two assumptions: first it is supposed that the most harmful resistance comes from obvious and noisy prejudice and that the more dangerous resistance of inertia and quasi-rational negation is unimportant; and secondly, it is supposed that workers in science are of course free from any resistive tendency but a rational conservatism. Each of these assumptions is an almost complete delusion.

The vociferous opposition met with by the ideas of Charles Darwin and of Lister probably did nothing to hinder the spread of these, and probably brought them within reach of a larger number of people capable of accepting them than would have been the case if the opposition had been well behaved. Again it was not noisy prejudice that caused the work of Mendel to lie dead for thirty years, but the sheer inability of contemporary opinion to distinguish between a new idea and nonsense. That his same inability may be shown even by the most eminent workers in science scarcely needs demonstration for anyone at all aware of the history of knowledge, but it may be illustrated by an anecdote which we owe to the third Lord Rayleigh and which is to be found in the delightful *Life* of that very great and wise man. J. J. Waterston was an engineer who interested himself in mathematical physics, and in 1845 wrote a paper on the molecular theory of gases which was ten or fifteen years in advance of his time and anticipated much of the work of physicists no less eminent than Joule, Clausius, and even Clerk Maxwell. The only contemporary judgement on this paper that survives is that of the referee of the Royal Society to whom it was submitted. He said, 'The paper is nothing but nonsense.' What Waterston might have accomplished if he had had the recognition and encouragement upon which this genius seems to have been unusually dependent, is beyond conjecture. He did not get them. His work lay in utter oblivion for forty-five years until it was exhumed by the pious efforts of Rayleigh. He himself lived on disappointed and obscure for many years, and then was overtaken by a yet deeper obscurity, for as the result of some strange accident or a long gathering impulse of despair, he disappeared and left no sign.—*The Collected Papers of Wilfred Trotter,* F.R.S. London, Oxford University Press, 1946, p. 26.

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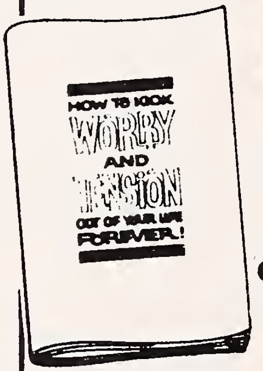

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160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, May 14, 1964

ORGANIZATION

This being the organizational meeting of the Council for 1964-65, Ralph L. Gilman of Storrs, president of the Society, called the meeting to order at 2:15 P.M. and served as chairman pro tem. After making certain opening remarks and introducing the new state officers and county councilors, Dr. Gilman declared the floor to be open for nominations for Chairman of the Council during the ensuing year. The name of Stevens J. Martin, Hartford, was presented and there being no other nominations, Dr. Gilman declared that Dr. Martin had been unanimously elected to the chairmanship for 1964-65.

REGULAR MEETING

I. Attendance

Present, in addition to the Chairman, Dr. Martin, were: Drs. Gilman, Cullen, Hess, O'Connor, Goldberg, Davis, Weise, Sr., Gardner, Pitock, Bradley, Grendon, Grant, Shepard, Ayres, Rogol, Ciccarelli, Seigle, Fabro, Abbot, W. E. Martin, Spitz. Also present were: Mrs. Lindquist, Mr. Burch and Dr. Richards. Absent were: Drs. Brandon, Caplan, Phillips, Hughes, Egan, Hastings, Major.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of April 22, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Maurice M. Hillman, New Haven (NHCMA)
Genesis F. Carelli, New Haven (NHCMA)

Resignation—Committee to Study Perinatal Morbidity and Mortality

It was VOTED to accept the resignation of Gillies G. Allard, Stamford, as a member of this Committee.

Resignation—Editorial Committee of CONNECTICUT MEDICINE

It was VOTED to accept the resignation of Gerald Klatskin, New Haven, as a member of this Committee, and it was further VOTED to appoint James R. Cullen, Hartford, to replace Dr. Klatskin on the Committee.

Resignation—Advisory Committee on Medicare Plan

It was VOTED to accept the resignation of Vincent J. Turco, Hartford orthopedist, as a member of this Committee, and it was further VOTED to appoint Martin L. Karno, New London orthopedist, to replace Dr. Turco as a member of the Committee.

Selection of 1964-65 Standing and Special Committees of the Council

Selections (election or appointment) were made for the 1964-65 standing and special committees of the Council. Changes from the 1963-64 selections are as follows:

(a) Liaison Committee with Connecticut Medical Service, Inc.—It was VOTED not to appoint this Committee for 1964-65.

(b) Subcommittee to Study and Revise the Bylaws —The Chairman was directed to fill all vacancies on the Subcommittee (caused by discontinuance of Council membership) and to designate the Chairman. Dr. Martin made the appointments, and the Subcommittee for 1964-65 is made up of the following:

James R. Cullen, Hartford, *Chairman.*
Jachin B. Davis, New Haven.
Frank K. Abbot, Waterbury.
David S. Hastings, Stafford Springs.
Stewart P. Seigle, Hartford.
Hilliard Spitz, New London.
William M. Shepard, Putnam.

(c) Subcommittee on Loan Fund—The Chairman was directed to appoint a replacement for Michael R. Scully, Bridgeport. The Subcommittee for 1964-65 is as follows:

Isadore S. Goldberg, Torrington, *Chairman.*

Richard F. Grant, Cromwell.
Payson B. Ayres, Greenwich.

(d) Advisory Committee to the Accident Prevention Study—It was VOTED to table action on appointing this Committee for 1964-65, pending receipt of information relative to the present status of the Accident Prevention Study (the General Manager to obtain this information).

(e) Committee on Committees—It was VOTED to reappoint the Committee as originally appointed in 1963, and to add new Divisional Chairmen elected by the House of Delegates on April 28, 1964.

(f) Advisory Committee on Cardiovascular Diseases—It was VOTED to reappoint the Committee, with one exception, William B. A. Bentley, Waterbury, who left the State.

The following committees remained unchanged from their 1963-64 composition:

Committee on Building Management.
Committee on Employees Pensions and Benefits.
Committee on Investment of Funds.
Committee on Corporate Practice of Medicine.
Representatives on State Operational Survival Plan.
Liaison Committee on Medical Education and Hospitals.
Committee on Indigent Fund.
Committee to Evaluate Committee and Staff Structure.
Committee to Meet with Commissioner of Welfare.
Special Committee on Resolution No. 2.

The following committees will be appointed, when necessary:

Committee on Arrangements.
Committee on Preliminary Study of Censorship Questions.
Committee on Preliminary Study of Nominations.

Appointment—Committee on County and Local Public Relations

It was VOTED to appoint William L. West, Derby, to membership on this Committee.

Date of Next Meeting

The Chairman selected Wednesday, July 1, 1964 as the date for the next regular meeting.

III. Old, New And Special Business

Directives from the House of Delegates—April 28, 1964

The Council took initial steps to comply with directives received from the recent meeting of the House of Delegates as follows:

(a) Resolution on General Practice — it was VOTED to direct the Chairman to appoint an ad hoc committee to implement this resolution, to designate Waldo E. Martin, Milford, as chairman, and to determine the number of members of the committee through consultation with Dr. W. E. Martin and the president of the Society, Dr. Gilman. The Chairman designated Dr. Waldo Martin chairman of the committee, and will appoint the other members of the committee after suitable consultation.

(b) Council's Report on "Hospital Costs and Accounting Procedures"—Since the Council was directed by the House of Delegates to continue its study of these matters, it was VOTED to request the Committee on Hospitals to act for the Council in continuing this study and to file a supplementary report with the Council when prepared to do so.

(c) CSMS Corporate Gift to COMPAC for Political Education Purposes—It was VOTED to table action in this matter, pending receipt of legal advice on the subject.

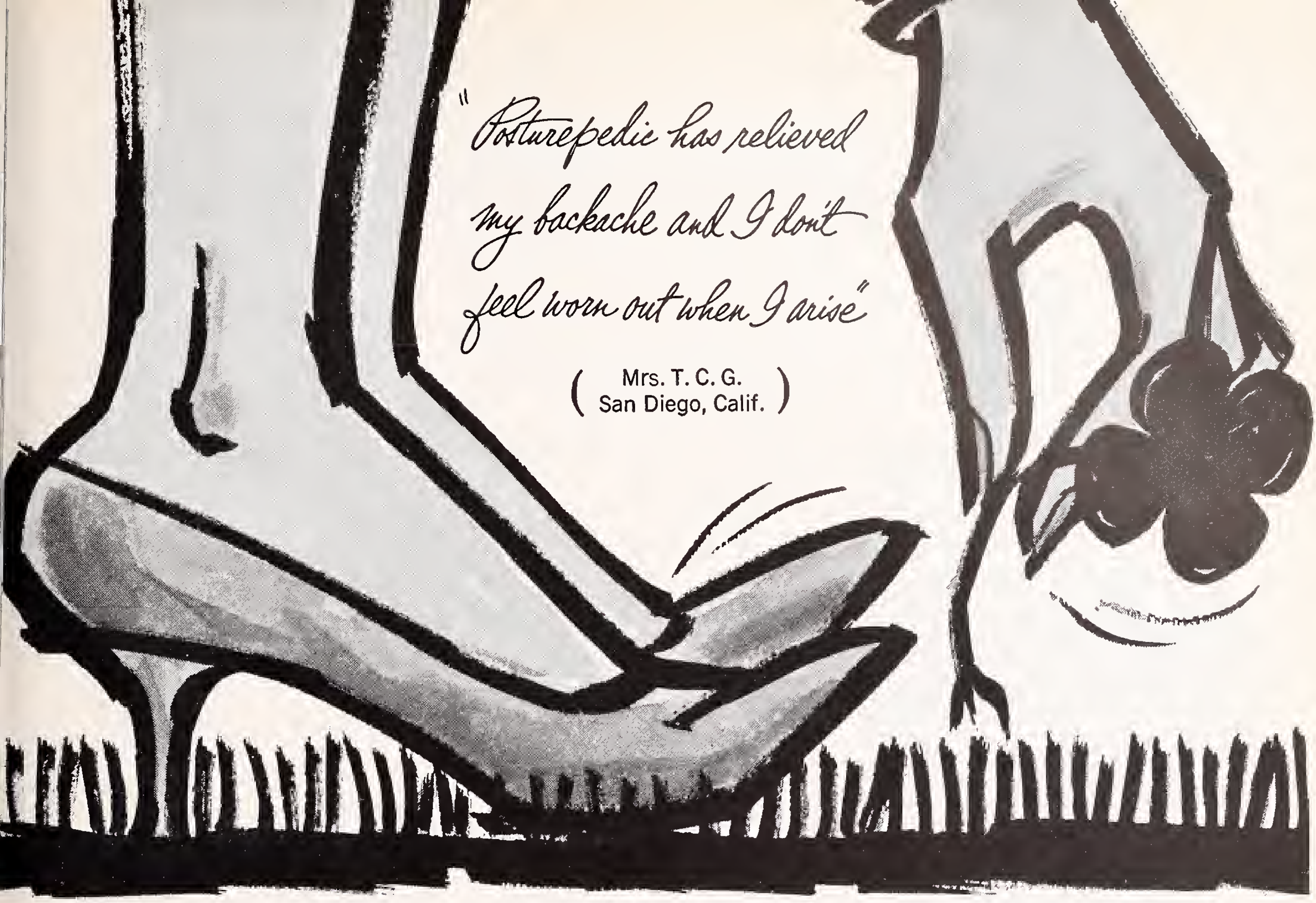
(d) HCMA Proposed Amendment to the Bylaws—As directed by the House of Delegates, it was VOTED to refer this proposed amendment on the Council's censorship powers to the Subcommittee to Study and Revise the Bylaws, in order that it may be considered with other related proposals for revising this section of the bylaws.

Report on WTIC Radio Program

Ralph L. Gilman, president, reported to the Council on his investigation of the nature and professional propriety of a commercially-sponsored WTIC radio program on which a member of the Society is featured on a continuing basis. It was VOTED to accept Dr. Gilman's report, which concluded that he believes "there is no cause to pursue this matter further, nor . . . that any type of censure is called for," and to send copies of the report and notice of this action of the Council to the member of the Society concerned and to the president of the Hartford County Medical Association.

Public Act 616—Chemical Tests for Intoxication

After reviewing excerpts from a legal opinion prepared by the Society's legal counsel on the question of the responsibilities assumed by a licensed practitioner in taking a blood sample for alcohol determination from a person in the custody of an arresting police officer, the Council took the following actions: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In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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(a) It was VOTED to adopt a resolution on P.A. 616 as follows:

"BE IT RESOLVED: That the Council of the Connecticut State Medical Society appeal to the members of the Society to accept whatever responsibility is properly asked of them by law enforcement officers and administrators in making chemical tests for alcohol intoxication of motor vehicle operators."

(b) It was VOTED to accept the printed excerpts from the opinion prepared by legal counsel.

(c) It was VOTED to publish both the resolution and the excerpts from the legal opinion in CONNECTICUT MEDICINE for the information of the Society's members, and to obtain a supply of reprints of this published material for future distribution on request.

(d) It was VOTED to request the Committee on State Legislation to prepare and have introduced at the next session of the General Assembly (1965) a bill to amend P.A. 616 as follows: "Such physician shall not be liable for damages, in any civil suit, for withdrawing such blood sample, except for negligence in the performance of such withdrawal."

The Medicare Contract for 1964-65

Robert R. Berneike, Chairman of the Advisory Committee on Medicare Plan, and Robert W. Hart, Coordinator for Medicare, joined the Council to outline the terms of the Medicare Contract for 1964-65 which had been submitted for renewal by the Office of Dependents' Medical Care. After determining that the Contract did not embody any of the changes previously recommended by the Society, but now included provisions for extending Medicare eligibility to the dependents of members of the NATO forces, it was VOTED not to renew the Medicare Contract for 1964-65 as submitted.

Membership in U.S. Chamber of Commerce

It was VOTED that the Society apply for organizational membership in the Chamber of Commerce of the United States, and to authorize payment of membership dues to the USCC for the current year, if the Society's application is approved.

Connecticut Medical Service, Inc.

1. It was VOTED to accept as information a letter from Mr. John Coolidge, president of CMS, dated May 8, 1964, addressed to Dr. Ralph L. Gilman, president of CSMS. Beyond expressing the regrets of the Executive Committee of the Board of Directors of CMS concerning "the decision of the House of Delegates to terminate sponsorship of CMS by the Connecticut State Medical Society," Mr. Coolidge notified Dr. Gilman of actions taken by the CMS Executive Committee as follows:

> "(a) Instructed the Committee on Bylaw Revision to recommend such changes in the (CMS) bylaws as are appropriate in view of the action taken by the (CSMS) House of Delegates in terminating its sponsorship of CMS.
>
> (b) Instructed the Executive Director to proceed without delay to make appropriate changes in CMS contracts, promotional literature and administrative forms to delete the phrase 'Sponsored by the Connecticut State Medical Society.'"

2. The Chairman reported that several of the physician members of the Board of CMS and members of the Medical Advisory Committee had requested an expression of the Council's views as to their obligation to continue or to terminate their services in those capacities, in view of the termination of the Society's sponsorship of CMS.

After discussion it was VOTED that it is the sense of the Council (a) that the question whether the termination of the Society's sponsorship of CMS does or does not impair the effective continuance of the services of the physician directors of CMS and the officers and members of the Medical Advisory Committee is a matter for individual consideration and decision, and (b) that the physicians concerned should feel no obligation to the Society one way or the other.

It was further VOTED that the President of each constituent county medical association be informed of these views.

3. It was VOTED that when the May issue of *Connecticut M.D.* is mailed out, the members of the Society be notified that extra copies of the "Statement" of the House of Delegates concerning CMS (on page 3 of the May issue) are available upon request from the Society's office for those members who may wish to use the Statement in the interests of furthering an accurate understanding of the Society's position.

4. It was VOTED that the Society's staff discontinue the service of certifying applicants for acceptance by CMS as Participating Physicians as to their being licensed to practice medicine in Connecticut.

5. It was VOTED to submit all the foregoing actions to legal counsel for review and approval prior to implementing them.

Payment of Legal Fees

It was VOTED to approve payment to Wiggin and Dana, New Haven, for legal services rendered in connection with the Society's controversy with CMS since January 1, 1964, and it was further VOTED to authorize the transfer of $3,000 from the General Fund to the 1964 budgetary allocation for legal and legislative counselling.

Appointment to the Connecticut Medical Examining Board

It was VOTED to request the Chairman to seek a meeting with the Governor for the purpose of reviewing with him certain questions which have arisen in connection with the appointment of a replacement for Joseph A. Fiorito (deceased) on the Medical Examining Board.

Acknowledgement—Assistant to the General Manager

In a letter addressed to the Chairman, Mrs. Lindquist expressed her thanks to the members of the Council and House of Delegates for the "lovely flowers and generous gift" which were presented to her on April 28, 1964, in recognition of her twenty years of service to the Society.

Authorization—Committee on Health Careers

It was VOTED to request Bernard F. Mann, Jr., Chairman of the Committee on Health Careers, to participate in a program of the American Hospital Association in Chicago, August 23, 1964, and to authorize reimbursement of Dr. Mann for usual expenses incurred by him in undertaking such participation.

Report—Chairman, Committee on State Blood Bank

It was VOTED to accept as information a report filed by John E. Thayer, Chairman of the Committee on State Blood Bank, on his recent meeting with representatives of the Connecticut Hospital Association and the Connecticut (American Red Cross) Blood Program. The essence of the report was that the Program's "Operating Reserves should be maintained equal to two months average expenses" and that "The Hospital Participation Fee should be reviewed annually with consideration being given to the necessary adjustment in multiples of 25¢ needed to maintain the Operating Reserve." The increase in the fee recommended for 1964 is from $3.00 to $3.25 per unit of blood used, although an operating deficit is anticipated even under the new rate. Dr. Thayer notes that the Committee on State Blood Bank suggested that a suitable adjustment of this nature should be made in a report filed with the House of Delegates several years ago.

Assignment—Committee on Aging

At the Council meeting of April 22, 1964, it was VOTED to accept a recommendation of the Committee on Aging that the Commissioner of Welfare be urged by the Council "that MAA people be processed separately, and on separate forms, from recipients of (general) public assistance in order to preserve their identity."

At this meeting, after discussion, it was VOTED to request the Chairman and other members of the Committee on Aging to seek a meeting with Commissioner Shapiro at which to explain to him, in person, the reasons for making this recommendation.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on May 14, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

The Society's Placement Service is in receipt of the following:

Hee R. Yoon, Age 32—M.D. Severance Union Medical College, Seoul, Korea 1957. Board eligible Otolaryngologist. Interested in group practice or partnership. Has Connecticut License.

BOARD ELIGIBLE PHYSIATRIST. Age 32—M.D. Tehran University, Iran, 1957. Interested in Physical Medicine and Rehabilitation. Has Connecticut License.

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FOR SALE. Ten room house and office, and exclusive, going, General Practice, in South Central Connecticut—open Hospital $35,000.

WANTED PHYSICIANS. Hartford, Middlesex, New London and Windham Counties.

WANTED. Pediatrician in New Haven County.

HARTFORD COUNTY. Internist's practice available, excellent location—abundant free parking.

FOR SALE. Long established medical practice and house, in Fairfield County.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN ST., NEW HAVEN.

1964 MEETINGS

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

October 29—181st Semi-Annual Meeting of the New Haven County Medical Association will he beld on Thursday, October 29, 1964, at Waverly Inn, Cheshire, Connecticut.

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FRIDAY, SEPTEMBER 25, 1964

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AROUND THE STATE

Yale University School of Medicine

Dr. Carlton C. Hunt, a neurophysiologist noted for his investigations into the spinal reflex mechanism, has been appointed Professor and Chairman of the Department of Physiology at the Yale School of Medicine.

Dr. Hunt resigned his current post as Professor and Chairman of the Department of Physiology at the University of Utah College of Medicine to accept his Yale appointment, which became effective on July 1.

He will succeed Dr. C. N. Hugh Long, Sterling Professor of Physiology, as department chairman. Dr. Long, who was Dean of the School from 1947-52, is stepping down after 12 years as chairman to devote full time to his research.

Dr. Hunt has been Professor and Chairman of physiology at the Utah College of Medicine since 1957. In his research, he has been concerned with the means by which nerve signals are initiated in the sensory organ receptors of muscles, the effect of these signals on the spinal cord, and their relevance to reflex control and movement.

He has found that muscles have sensory organs that are responsible for maintaining a state of excitability in the nerve cells that control muscle contraction.

He has also studied sensory mechanisms in the skin, transmission of nerve impulses across the synapse, or gap between nerve cells, and the mechanism of excitation in the spinal cord.

Dr. Hunt was born in Waterbury, Connecticut, on August 11, 1918. He was graduated from Columbia University with a B.A. degree in 1939, and from Cornell University with his M.D. in 1942.

After a year as an intern at New York Hospital, he entered the Army, and served as a medical officer for three years. He returned to New York Hospital in 1946 as an assistant resident in medicine.

He served as a Research Fellow, and later as Instructor, in Pharmacology at Cornell University Medical College from 1946 until 1948, when he was named a Senior Fellow in Neurology of the National Research Council at Johns Hopkins University.

During 1951-52, he held an appointment as Assistant Professor of Physiology and Physiological Optics at Johns Hopkins. In 1952, he was named an Associate of the Rockefeller Institute for Medical Research, and in 1955, Professor of Physiology at Albert Einstein College of Medicine.

During the 1962-63 academic year, he was a Visiting Professor at University College, London. He belongs to the American Physiological Society and the Harvey Society, and is the author of more than 30 scientific papers in pharmacology and neurophysiology.

Board Of Governors Meeting New Haven County Medical Association

May 20, 1964

The Board of Governors of the New Haven County Medical Association held a meeting on May 28, 1964, at the quarters of the County Association, 362 Whitney Avenue, New Haven.

Items from the latest meeting of the Council and current in the County were on the Agenda. Lively general discussion, a feature of these meetings, preceded the vote on these problems.

The Ad Hoc Committee for Review of Third Party Payments complaints under Dr. Kurt Pelz, reported happy solutions brought about, without pressure, and by the co-operation of all parties concerned.

In a matter of a complaint against a non-member physician practicing in our County, it was felt this did not come under our jurisdiction. There are other avenues of redress for the patient.

It was voted we will no longer supply nominations to the Medical Advisory Board of CMS unless and until sponsorship is resumed by the Connecticut State Medical Society. Present incumbents may take such action as they desire, as they are now strictly on their own.

At dinner following the meeting, Dr. R. L. Larson of Hartford and Travelers Insurance Company presented the case of Major Medical Insurance coverage by insurance companies. Discussion from the floor was able to show the other side of the coin was still quite shiny.

New Chief Of Maternal And Child Health

Estelle Siker, M.D. of New London, Connecticut, has been appointed Chief, Maternal and Child Health Section, Connecticut State Department of Health by the Public Health Council, announced Franklin M. Foote, M.D., Commissioner, Connecticut State Department of Health. Dr. Siker has served as a physician in the Crippled Children Section of the department since 1956. She is completing work for the Master of Public Health degree, at Yale University School of Medicine in June, 1964.

Dr. Siker was Chief Pediatrician in the Montefiore Hospital Medical Group of the Health Insurance Plan in New York City in 1949-1953. Before that she served on the staff of Grasslands Hospital, Valhalla, New York 1943-1946, having received her M.D. degree from the Women's Medical College of Pennsylvania in 1943.

The new chief of the Maternal and Child Health Section is certified by the American Board of Pediatrics, is a member of the American Academy of Pediatrics, the American Medical Association, and of the Hezekiah Beardsley Pediatric Society. She is the author of "The Role of the Pediatrician in the Family Health Maintenance Demonstration," in the Milbank Foundation Report 1953. Dr. Siker is the wife of Rabbi Henry O. Bernstein. The Bernsteins with their two sons will soon make their home in Hartford.

In becoming chief, Dr. Siker succeeds Louis M. Spekter, M.D., who recently retired after 25 years of service to take a position in the Children's Bureau, Washington, D. C.

Quackery

The health quack and the food fad quack have been around since the beginning of time, and they'll probably be with us for a long time yet. They'll be here as long as quackery is profitable. And quackery will be profitable as long as we continue to fall for it.

Some experts have estimated that Americans spend a billion dollars a year on useless cures, mechanical gadgets, food fads and other quack gimmicks. For instance, there is no sure cure for arthritis, and yet we spend a quarter of a million dollars a year on "cures." Some cancers can be cured by medical experts, but many cannot. But we spend $50 million a year on useless cancer "cures." Doctors will tell you that most of the $150 million a year spent on self-prescribed laxatives is either wasted or actually harmful.

At best the quacks waste our money. And sometimes they can cause us to delay seeking proper treatment for a serious condition that gets worse as time goes by. Some of the quack gadgets and medicines are downright dangerous.

Your doctor, both individually and through his professional organizations such as the American Medical Association, wages constant war on quacks. So do several government agencies at a national level and many state and local government bodies.

How can we as individuals avoid being taken in by a quack? The modern day medicine man is a slick operator, but there are a few guidelines that will at least cause us to take a second look at his proposition. Through long years of experience, the AMA's Department of Investigation offers six ways to spot a quack—

- If he uses a special or "secret" machine or formula he claims can cure disease.
- If he guarantees a quick cure.
- If he advertises or uses case histories and testimonials to promote his cure.
- If he clamors constantly for medical investigation and recognition.
- If he claims medical men are persecuting him or are afraid of his competition.
- If he tells you that surgery or x-ray or drugs will cause more harm than good.

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OBITUARIES

Wilbert E. McClellan, M.D.
1881 - 1964

Dr. Wilbert E. McClellan, an ear, nose and throat specialist, died May 24, 1964 at St. Francis Hospital, Hartford, after a brief illness. His age was 82.

Born in Almonte, Ontario, Canada, he received his medical degree from Toronto University, Faculty of Medicine in 1904.

Following his graduation in medicine, he attended London College where he followed an intensive study of neuro-anatomy. In 1908 he was a resident at the Manhattan Eye and Ear Hospital. Following an invitation from members of the staff of St. Francis Hospital, he came to Hartford and in 1910 opened his office. He became attached at once to the staff of St. Francis Hospital and continued this relationship until the time of his death. As head of an ear, nose and throat service, he was able to make use of his advanced training, particularly at that time when infections of the mastoid were so frequent and often called for surgical treatment.

During the early years of the century, he published a number of scientific papers including one entitled, "Pulsating Exopthalmos Due to Aneurysm of the Internal Carotid," which appeared in the *Journal of the American Medical Association* in May 1911. Another of his interesting papers entitled, "Lateral Sinus Thrombosis," appeared in the *Yale Medical Journal* of December 1911.

He was a diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, a member of the Royal College of Surgeons of London, England, a member of the American Academy of Ophthalmology and Otolaryngology and a Senior Member of the Triological Society. He was consultant to the Institute of Living, Newington Home for Crippled Children, New Britain General Hospital, McCook Memorial Hospital and Cedarcrest Hospital.

Dr. McClellan was a student of medicine throughout his professional life. He gave freely of his talents and skill to his fellow doctors and like Chaucer's Oxford Clerke, "who would gladly learn and gladly teach," he contributed much to the growth of Saint Francis Hospital.

Dr. McClellan is survived by his wife, Helen Pease McClellan; a son, Wilbert E. McClellan Jr. of Groton; a daughter, Mrs. W. Leslie Smith of West Hartford.

EDWARD J. WHALEN, M.D.

Joseph S. Paladino, M.D.
1898 - 1964

Dr. Joseph S. Paladino was born in Florida, Sicily in 1898 and came to this country at the age of 14 years. He died at the Morton Plant Hospital, Clearwater, Florida following a brief illness.

He received his B.A. degree from Colgate University, Hamilton, N.Y. and a D.D. degree from Colgate at Rochester N.Y. He entered Yale Medical School in 1922 and the following year transferred to Boston University where he received his M.D. degree.

Dr. Paladino was a member of the American Medical Association, the Connecticut State Medical Society, the Hartford County Medical Association and Hartford City Medical Society.

He devoted his entire professional career to a general practice in Hartford, Connecticut and won the highest respect of his patients and colleagues. He was a dedicated member of his community which he served faithfully and well until his retirement in 1962. He will be missed by all.

He is survived by his widow Mrs. Winifred Karn Paladino of Clearwater, Florida. Three daughters, Mrs. Robert Shoup, Wychoff, New Jersey; Mrs. Carl Hampton, Framingham, Mass., Mrs. Duane Belden, Winchester, Mass., and four grandchildren. Also, a brother Frank Paladino, Rome, Italy and a sister Mrs. La Raja of Hartford, Connecticut.

ROBERT H. OSMOND, M.D.

In Memoriam

Merriman, M. Heminway—Waterbury; Columbia College of Physicians and Surgeons, 1906. Dr. Merriman was a prominent ear, nose, and throat specialist in the Waterbury area for over a quarter of a century. He was associated with Waterbury Hospital for 24 years. Dr. Merriman was a former trustee of Taft School, Watertown, and recipient of the Citation of Merit, the highest accolade of the Taft School Alumni Association. He was a past president of the Waterbury and New Haven County medical societies. Dr. Merriman was a member of the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, the Waterbury Medical Association, and the New York State Medical Society. He was a fellow of the American College of Surgeons and a Diplomate of the American Academy of Otolaryngology. He was for many years a member and later an honorary member of the staff of the Waterbury Hospital. Dr. Merriman was past president of the Watertown Sons of the American Revolution and a member of the Society of Colonial Wars of the State of Connecticut. Dr. Merriman died May 28, at the age of 86.

AMA Awarded To Rene Jules Dubos For Scientific Achievement

Professor Rene Jules Dubos, Ph.D., of the Rockefeller Institute, New York City, noted philosopher, pathologist and microbiologist, received the Scientific Achievement Award of the American Medical Association in June.

The award, consisting of a gold medal, was established in 1960 to honor non-physician scientists, who have done outstanding work. It was presented at the AMA's annual convention in San Francisco during presidential inaugural ceremonies in the Grand Ballroom of the Fairmont Hotel.

Dr. Dubos is one of the world's great bacteriologists. His contributions to medical science include development of a rapid method for growing tubercule bacilli in submerged cultures; inquiries into the mechanisms of acquired immunity and resistance to infection, with special stress on tuberculosis, and the discovery of the antibiotic tyrothricin.

Dr. Dubos was born in Saint Brice, France, in 1901. He attended school in Henonville and studied at the College Chaptal and Institut National Agronomique in Paris. He entered his scientific career almost by chance.

"I got a job as an assistant editor on the staff of the International Institute of Agriculture in Rome, a section of the League of Nations," he recalls. "My job was to prepare abstracts for a journal of agriculture. Through a miraculous accident, I acted as guide for Dr. Selman Waksman and got to know him. When I decided to go to the United States, I found that Dr. Waksman and I were sailing on the same ship."

It was through Dr. Waksman, later one of the codiscoverers of streptomycin, that Dr. Dubos went to Rutgers University in 1924 and worked as a research assistant and instructor in bacteriology. In 1927, he joined the staff of the Rockefeller Institute, where he has remained, except during 1942-44, when he was George Fabyan professor of comparative pathology and professor of tropical medicine at the Harvard University Medical School.

Special Notices

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A full-time, five-day course in occupational health for registered professional nurses in industry will be offered beginning Monday, November 9, 1964, by the department of environmental medicine of New York University Medical Center, in cooperation with the American Association of Industrial Nurses. The course is limited to nurses with experience of five years or less in occupational health.

The program will be under the direction of Dr. David H. Goldstein, professor of environmental medicine. Sara P. Wagner, R.N., will serve as coordinator for the nurse faculty. This is the ninth consecutive year that the course has been given.

Instruction will consist of lectures and conferences given by the combined medical and nursing faculty of the Medical Center. Subjects to be covered during the week include: occupational health nursing as viewed by management, the physician and the nurse; environmental hazards; safety; mental health, individual and group behavior in an industrial setting; counselling and interview techniques; legal aspects of nursing in industry (malpractice and workmen's compensation); rehabilitation; and retirement and the problems of older workers.

Tuition will be $75. Course No. 484.

Applications should be sent to the Office of the Recorder, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, N. Y.

BOOK REVIEWS

ATHEROSCLEROSIS MECHANISMS AS A GUIDE TO PREVENTION by Campbell Moses, M.D., Lea and Febiger Company, Philadelphia, Pennsylvania, 1963, 239 pp. $8.00.

Reviewed by: LOUIS H. NAHUM

There are several questions a physician is always consciously or unconsciously concerned with, when atherosclerosis is considered. One is whether a patient has or is destined to develop this disease. Another is whether once the disease has been identified, if it can be arrested or reversed. To derive answers to this question, Dr. Moses has written this comprehensive monograph which is based upon his own researches and an extensive survey of 1250 articles from the literature. In this sense, this book contains an analysis of all the known factors that have a bearing upon atherosclerosis.

It is time for such a volume because it required some authority like Dr. Moses to help dispel existing confusion caused by many contradictory reports on hyperlipemia, polyunsaturated fats, heredity, obesity and exercise. Since this book has been written even hyperlipemia as distinct from hypercholesteremia has lost its importance.

The factors which Dr. Moses considers are, metabolic, hormonal, hereditary, dietary, smoking, hypocholesteremic drugs, exercise, emotion and others. What is not considered is infection, toxins. What is somewhat blurred is the role of the elastic lamella in protecting against atherogenesis. A most valuable concept developed by DeBakey that atherosclerosis itself may be self-limited and that the ravages of this disease namely thrombosis may be and should be considered in any form of prevention, will undoubtedly be considered in a subsequent edition.

Dr. Moses discusses hypocholesteremic drugs such as sitosterol, nicotinic acid, pyridoxin, neomycin, benzinalacene, heparin and triparanol. The last receives a full one and one-half pages in a chapter of five and one-half pages. Since tripanol has been eliminated from its role in treating hypercholesteremia, it has been relegated to the laboratory as a biochemical tool and hardly merits extensive consideration.

The chapter on smoking is well written, clear and unmistakable. But a final sentence, that "if cigarette smoking cannot be reduced without disastrous sequelae (p. 179)" is distinctly an anticlimax to his general thesis that smoking is a great hazard both in heart and lung disease.

In this discussion of exercise and its effect on thrombosis in a coronary artery the position is not too clear; we know that a thrombus takes time to mature, an infarction is not a beginning but an end of a process, and probably cannot be related to an immediate antecedent event.

Diet and atherosclerosis is the longest and most practical of all the chapters, consisting of eighteen pages and filled with practical common sense upon this difficult subject. He accepts as his thesis a report of the Central Committee for Medical and Community health of the American Heart Association.

We are indebted to Dr. Moses for this excellent review of a disease from which over half of our patients and ourselves are destined to suffer. If answers are not yet clear enough to all the difficult aspects of this obscure disease, at least we know after reading this scholarly work, where we are at present and where the future is tending. It should be "must reading" to all students, physicians, physiologists, and biochemists.

HANDBOOK OF LEGAL MEDICINE by Alan R. Moritz and C. Joseph Stelter. C. V. Mosby Co., St. Louis, Missouri, 2nd edition, 1964, 239 pp. $5.75.

Reviewed by: ROY N. BARNETT

This small volume, according to the author's preface, "deals with two more or less distinct aspects of law-medicine relationship." One is legal or forensic medicine, the other medical jurisprudence which "concerns the legal responsibilities of the physician with particular reference to those arising from the physician-patient relationship."

The work contains a considerable body of well-presented material and has a common-sense approach. The main problem is: To whom is this book directed? The general approach is probably to the medical student taking a brief course in legal medicine and medical jurisprudence. It might also be useful to a law student needing survey material about the same general field. It is certainly not adequate for the medical examiner, coroner, pathologist or claimant's lawyer.

The format is pleasing and easy to read, with some clever and pointed drawings. There is considerable waste space due to excessively brief chapters occupying only a portion of a page. At the end there is a curious glossary which tells the non-physician what *agglutinin* and *prothrombin* mean, and the physician about *demurrers* and *noncupative wills.* Some of these terms do not appear in the body of the book so that apparently the authors intend this as a 12-page all-purpose index to medicine and the law.

The proof-reading is about average, such difficult words as *privilege* and *physical* having been misspelled. I don't know whether the modern systems of teaching children to read have blinded the graduates to improper spelling, or whether the flood of written words has inundated the proof-readers and editors but the number of errors in even the best-written and most thoughtful books seems to be increasing sharply. Besides being unseemly this flaw shatters one's faith in the infallibility of the author's thoughts, even though he is rarely to blame. Alas, this very journal is all too vulnerable in this area; otherwise we might lead a great national movement to be called SPELL (Society Pursuing English Language Literacy).

This volume is recommended primarily to undergraduate students of law and medicine.

THE FAMILY AND HUMAN ADAPTATION by Theodore Lidz, M.D., International Universities Press, New York, New York, 1963, 113 pp. $3.00.

Reviewed by: LOUIS H. NAHUM

This book contains three lectures delivered at Tulane University on February 23rd and 24th, 1961 and are called the Mona Bronfman Sheckman Lectures in Social Psychiatry. The thesis of all the lectures is that the family is a unit and the

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action of any member affect all. From psychoanalysis we have learned of the importance of maternal attitudes and also of parental attitudes towards feeding, bowel training, childhood sexuality, sibling rivalry, and specific ways in which parental attitudes contribute to ego and super-ego relationships. It was Freuds discovery of the edipal configuration that really opened the way for study of the family dynamics. Thus we find attention was formerly focused as parent-child relationship, not on parent-parent relationship as it affects the child.

The author points out that all studies starting with an individual must meet up with sociologic study of the family as a basic unit and so he, in these lectures, explores the critical role of the family in human adaptation and integration. A comprehension of the family role should clarify the interaction between man's genetic inheritance and his cultural heritages.

The concepts which are considered in these lectures arose from studies of families of schizophrenic patients. Something seems to have gone amiss in the integration of these families. Something essential to the proper development of their children. Freud derived normal psychodynamic factors from a study of the neuroses. Professor Lidz derives normal requirements of the family operation from a study of a disrupted group of families in schizophrenia.

His thesis then is, that if schizophrenia is not caused by some process that disrupts the integrative capacities of the brain, (some believe there is a biochemical basis for it) then it could be due to maladaptation and malintegration due to deficiencies in acquiring instrumental techniques and language. He analyzes the importance of the marital interaction of parents upon the personality development of their children. He examines the central role of language—"the word, the tool of tools"—in human adaptation and the parents role in nurturing and directing the childs linguistic abilities. The child is dependent upon learning useful and valid meanings to enable him to be adaptable to new conditions.

The author believes that the ability to control and channel basic drives, to understand "self," to direct the self towards future goals and indeed ego functioning in general are inherently related to the acquisition of a language and the "categorization of experiences through words." And so he discusses the various ways in which parents impede language development, foster distrust of the ability of verbal communication, and thus indicate confused and distorted meanings. Of course, the end result of such a process is found in schizophrenic children who conceptualize poorly, distort meanings, and suffer ego fragmentation.

The book has opened a pandora's box filled with problems for psychologists and psychiatrists to investigate further. Nowhere can one find a clearer presentation of the role of the family in cultural evolution, at least in a society such as ours. The author has been influenced by Whorl and Sapir with their emphasis upon language as a tool for studying cultural evolution and of course, by Freud. It is charmingly presented and scholarly in its broad overview of human cultural evolution. It can be read again and again, by all physicians, educators, social workers and intelligent laymen. It will not easily go out of date for it lays a foundation for concepts, hypotheses and areas for further verification. In this sense it can be called a classic in its field.

HEREDITY AND HUMAN LIFE. Hampton L. Carson. Columbia University Press, New York and London, 1963, 214 pp. $5.00.

Reviewed by: MAX CAPLAN

Although we doctors are confronted with the vagaries of genetics every day, only recently have we learned of its role in a great many diseases. Literally hundreds of disease processes ranging from diabetes to disseminated lupus, from abortion to alcoholic cirrhosis, from polyposis to porphyria, from hypertension to hemochromatosis are influenced by genetics in large measure and students of this fascinating subject are accruing more and more scientific evidence to show that very few of our illnesses are outside its pale.

A great deal of this knowledge is the concern of all of us and not merely the doctors. It is important to be able to explain the rudiments of heredity to our patients and to all those who want to understand them. For those who want to get a simple text which is easily understandable, interesting reading, and excellently presented, this little book "Heredity and Human Life" by Hampton L. Carson can be warmly recommended. He skillfully uses diagrams, pictures, simple drawings, and homely examples to explain many of the facets of hereditary information, stability of the hereditary material, combinations and recombinations of genes, heredity and environment, etc. The problems which are caused by mutations both natural and due to ionizing radiation are discussed.

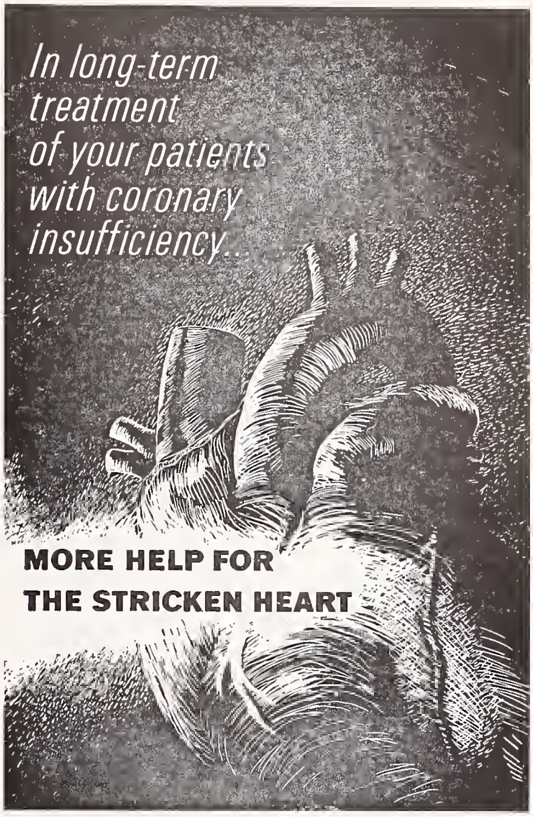
The second half of this book traces the origin of the Human species. Professor Carson skillfully traces the ancestors of man during the last 25 million years. He takes us from Africa where the evidence shows we began thru our prehistoric migrations. As he proceeds, he emphasizes the relative unimportance of group differences in heredity and shows the fallacy of judging brains from cultures.

THE PRACTICE OF COUNTRY RADIOLOGY by Donald de Forest Bauer, M.D. Charles C. Thomas, publisher, Springfield, Illinois, 1963, 257 pp. $11.75

Reviewed by: SIDNEY L. CRAMER

One could not help but admire the intense desire of the author to tell his story. He was determined that one and all should benefit from his experiences which he considered unique and valuable.

Doctor de Forest Bauer had practiced for many years in small communities in Oregon and California where he had but limited access to the more esoteric equipment in larger hospitals. Also his contacts with internes and residents in radiology had been limited. Because of his remoteness, he felt he qualified as a "country radiologist," and described his experiences as such. The book would make interesting reading if it remained as an autobiography of a radiologist practicing in rural areas. Instead, the author assumed that his experiences were characteristic of all that were to follow in the discipline of radiology if practiced away from a medical center, and the book, thereupon, became an instruction manual on "how to do." No subject was too small or unimportant upon which to pontificate and philosophize. Paragraphs were devoted to detailed instruction on how to enter-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tain the referring physician; to keep check stubs for investigation by the Internal Revenue Service; to buy automobile insurance; and to fabricate a home-made enema can.

This elaboration of minutiae coupled with the "do as I tell you" tone proved annoying to the reader. Perhaps the novice in radiology might find some worthwhile instruction within its pages, but he would do better if his time were used in other reading.

THE ELECTROCARDIOGRAM AND CHEST X-RAY IN DISEASES OF THE HEART, Arthur A. Master, M.D., Richard P. Lasser, M.D., Isadore Rosenfeld, M.D., and Efrim Donoso, M.D. Published by Lea & Febiger, Philadelphia, Pennsylvania, 1963, 565 pp. $21.00.

Reviewed by: ARTHUR A. RUBIN

Dr. Master and his associates have attempted to present the roentgenographic, electrocardiographic, clinical and pathological findings in a wide variety of cardiac diseases.

As explained by the authors in the preface, physiological abnormalities are predicted from the characteristic X-ray and electrocardiogram. While not intended as a textbook, there is a brief, but concise review of the normal X-rays, angiocardiogram and electrocardiogram.

The chapter on cardiac chamber enlargement reviews the characteristic electrocardiographic patterns and X-ray images of different chamber enlargement and their correlation with various hemodynamic mechanisms responsible for the chamber enlargement.

The concept of systolic and diastolic overload is discussed and its electrocardiographic characteristics presented. There is an excellent discussion of the characteristics of the P-wave in various type of atrial enlargement.

The remainder of the book deals with specific disease entities in terms of their clinical pathophysiological and roentgenologic as well as electrocardiographic characteristics.

In general, the reproductions of the X-rays and the electrocardiograms are excellent. There are liberal examples of all the common and most of the uncommon cardiac diseases. For the physician who is not a cardiologist, the book presents a great number of varied cases with excellent descriptions and illustrations, together with the author's interpretations of the electrocardiographic reading.

The major disturbing feature of the book is the effort of the authors to correlate the X-ray, electrocardiogram and the pathological findings. In so doing, there appears to be a tendency to over read minor electrocardiographic changes to conform with X-ray or clinical findings. This gives the impression that most cardiac diseases have a rather specific electrocardiographic and x-ray pattern and that specific disease entities can be diagnosed by these ancillary diagnostic procedures. While experienced cardiologists, such as the authors who utilized all means of diagnosis, may be able to do this, the average physician is likely to read more into the electrocardiogram than is justified.

However, despite the above shortcomings, the book should be a useful reference for all physicians who are interested in the diagnosis of heart disease.

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THE SMALL INTESTINE: ITS FUNCTION AND DISEASES by Thomas W. Sheehy, M.D. and Margin H. Floch, M.D., Hoeber Medical Division, Harper and Row, New York, 1964, 479 pp., 129 illustrations.

Reviewed by: ROY N. BARNETT

This new monograph, devoted to the small intestine, is indeed a useful addition to the medical literature. It deals with a portion of the anatomy whose size, noisiness and function impress even the layman, but one commonly ignored in medical literature.

The work is divided into two major sections, the first dealing with function and diagnostic testing, and the second with the diseases of the small bowel. In the first section are chapters on anatomy, histology and histopathology; carbohydrate, lipid and protein metabolism; erythropoiesis and anemia; motility, pharmacology and electrolytes; and diagnostic radiography. There is gathered together here in very readable fashion a wealth of up-to-date information on many subjects of very basic interest. Some of these, such as performance and interpretation of peroral small bowel biopsy, the xylose tolerance test, and the anemias related to intestinal dysfunction are discussed extensively because they are not familiar to physicians generally.

In the second section the diseases are divided into malabsorption syndromes; diffuse lesions of the intestinal mucosa; post surgical problems; vascular diseases; infectious diseases; parasitic diseases; neoplasms; and diseases of unknown etiology. Particularly intensively described because of the the authors' great interest in them and because their collaborative studies were carried on chiefly in Puerto Rico are sprue and parasitic diseases. Whipple's disease also receives extensive coverage. Cholera is very well discussed; although the United States is presently free of this alarming disorder it could gain entrance at any time and we should have some basic knowledge of its diagnosis and treatment.

It would be surprising if the reviewer agreed in every way with the statements made and the relative importance attributed to various diseases. For example, intussusception receives 14 lines and acanthocytosis 23 although in the practice of most physicians the former is far commoner. There is no mention of the involvement of the small bowel in ulcerative colitis although this is not rare. The danger of appendectomy done during the course of acute ileitis is vastly overrated at one-third of all cases. Nor is there no proof that duodenitis accompanies duodenal ulcer; acutally this is so frequent that documentation has been considered unnecessary. These criticisms do not detract from the value of the book; it may well be better to expound on a rare condition which the reader never heard of than to discuss material which he already knows well.

The publisher has done a most pleasing job. The paper, typography and illustrations are of the highest calibre. The larger borders and large spaces between paragraphs make for great ease of reading. The proofreading is good. I believe this volume is well worth owning for internists and pediatricians particularly.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

The Specialties in General Practice. Edited by Russell L. Cecil, M.D., Third edition, W. B. Saunders Co., Philadelphia, London, 1964, 676 pp. $17.50.

Pediatric Ophthalmology. Edited by L. Byerly Holt, M.D., F.I.C.S., Lea & Febiger, Philadelphia, 1964, 403 pp., 64 illus. $12.00.

The Theory and Practice of Medicine. Introduction by Emerson Crosby Kelly, M.D., New York: Philosophical Library. $7.50.

Outline of Physiology. L. L. Langley, Ph.D., LL.B. Professor of Physiology University of Alabama, McGraw-Hill Book Co., Inc. New York, Toronto, London. 1961, 564 pp. $5.50.

Cardiovascular Surgery 1963. Council on Cardiovascular Surgery American Heart Association Scientific Sessions. Edited by F. A. Simeone, M.D. The American Heart Association, Inc., New York, 1964, 180 pp. $3.00.

Business Management of a Medical Practice. Bernard D. Hirsch, LL.B., Director, Law Department, American Medical Association, Chicago, Illinois, The C. V. Mosby Company, St. Louis, 183 pp. $7.75.

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Mouth Cancer In Connecticut

During the seventeen-year period from 1935 to 1951 an average of 143 persons died each year in Connecticut from cancer originating in the mouth. In other words, over two thousand individuals died during that period from mouth cancer. In addition, the crippling physical and psychological effects which remain with hundreds of individuals who were treated and survived, may not in good conscience be overlooked in defining the problem. Restoration of function confronts both the physician and patient with many problems. Frequently extensive surgery is required, as well as other rehabilitative techniques.

Symptoms Of Mouth Cancer

Seldom are the first symptoms of mouth cancer either distressing or painful. Pain may be absent for a period of weeks, and sometimes months. Even with the absence of pain, it is only during the early stages of mouth cancer that treatment may result in a cure.

When cancer appears on the tongue, gum or any other area of the mouth, the individual may suspect that the teeth are involved and he may seek professional help from a dentist. Therefore, it is the dentists who are in a particularly advantageous position to play a leading role in early detection of mouth cancer. Many individuals can be greatly indebted to dentists who have recognized the potentially dangerous nature of such tissue changes in the mouth, and who have given sound advice as to the need for early investigation of those changes.

Early Detection Of Mouth Cancer

The time element is of utmost importance in preventing deaths which result from mouth cancer. A small growth, if neglected, may within just a few weeks spread to other areas of the body, resulting in new growths which may become incurable. For the early detection of mouth cancer, three basic techniques are available:

1. A comprehensive mouth examination—this includes a critical inspection of all tissues of the mouth.
2. Oral cytology (the oral smear) —this technique is simple, practical and reliable. However, it is a supplement to, and not a replacement for, the biopsy technique.
3. The biopsy—from which the final diagnosis of mouth cancer is routinely made.

Public education is increasing the number of patients who consult physicians and dentists promptly; professional education and interest has made early diagnosis increasingly successful. To make a concerted effort to decrease the number of persons who die each year from mouth cancer is not only a commendable effort but a reasonable goal of both the medical and dental professions in Connecticut.

It can be achieved if professional personnel are alerted to the need for routine comprehensive oral examinations which include a critical inspection of all soft tissues of the mouth, and particularly of all lesions of the mouth, regardless of their clinical appearance.

The value of such procedures can hardly be compiled or measured; the exact number of lives saved, and the amount of human suffering and disfigurement can only be estimated.

In addition to reducing the number of deaths from oral cancer, increased awareness of this problem would reduce the varied and severe psychological and physical problems resulting from inadequate rehabilitation procedures. One frequently sees people who were fortunate enough to be cured of oral cancer, but who are either unable or ashamed to appear as acceptable and working members of society because of the mutilating effects of the disease. It is in this area as well that the collaboration of the dentist and the physician is of immeasurable importance.

Post-Birth Changes In Circulation Triggered By Blood Oxygen Pressure

Oxygen pressure in the blood is the "switch" that changes the circulatory patterns in babies within minutes after they take their first breath. As a result of this finding by Dr. Nichols Assali and his associates at the University of California in Los Angeles, a way may eventually be found to treat, without surgery, one *of the most common inborn heart defects, "patent ductus arteriosus."*

When the baby is in the womb, its oxygen needs are supplied by the mother's blood and the baby's own blood is routed away from its unexpanded lungs through the vessel called the ductus arteriosus. After birth this bypass shrivels and disappears. If it does not— as in several thousand infants born each year—useless recirculation of blood between the heart and lungs takes place, adding to the heart's work and slowing the child's growth. Surgery can close an open duct; in fact, the modern era of heart surgery began in 1938 with an operation of this type.

In his research (aided by the American and Los Angeles County Heart Associations) Dr. Assali found that *as normal infants begin to breathe, more* *and more oxygen is absorbed into the blood stream and oxygen pressure rises. When a critical pressure is reached, the ductus shuts.* Generally closure takes place within the first half hour after birth. After a time in certain cases the ductus loses its sensitivity to oxygen and does not respond to elevated pressures.

Any condition that prevents the newborn's lungs from being exposed to sufficient amounts of oxygen may interfere with closure. Thus premature babies, whose lungs are not fully developed, are particularly prone; so too are children born in the Peruvian Andes at altitudes of 16,000 feet or more where the air is extremely thin (oxygen-poor). With the normal closure mechanism now clarified, the search is under way for methods of raising the oxygen pressure of the blood in newborns or otherwise stimulating duct closure.

Maybe Nature Never Intended The Sexes To Converse

The reason husbands and wives don't talk to each other may be because nature never intended the sexes to converse.

"In the beginning it was sufficient for the male to bring home the kill, his mate to cook it, with no exchanges between them beyond an occasional 'Ugh,'" according to an article in the current Today's Health magazine, published by the American Medical Association.

"Deep in the male animal are bred thousands of centuries of regarding women as slaves. And for hundred of years even after civilization began, in most societies men ruled the oral roost.

"Small wonder then that having finally burst their bonds, women are anxious to make up for lost time. Or that after such long conditioning, men regard this comparatively recent manifestation, the articulate woman, with a mixture of amazement and distress."

Rather than get into serious discussions with his wife, a man prefers to let well enough alone, according to the article. This is especially true of a man whose parents may have practiced reserve with each other, so that he wasn't accustomed to hearing much free expression as a child.

"So he listens guardedly, if at all, to his wife's hopeful outpourings. He does not make the mistake of encouraging her by his own comments, which might lead to a genuine discussion. By his demeanor he registers polite discomfort, if not outright resistance. And at the first graceful moment he escapes."

If women are sensible, they make the best of it, the article continued. The wife shouldn't blame her husband for something he can't help. She shouldn't expect too much, but she shouldn't stop trying altogether. She can always pick up the phone and call a friend.

The same sexes converse most honestly and comfortably together anyhow, the article concludes.

Quicker Way Found To Screen Babies For Phenylketonuria

A quicker method has been devised for screening newborn infants for phenylketonuria, a hereditary disease which can cause mental retardation.

A determination can be made within 16 hours following a laboratory test on a blood sample from a baby's heel, according to a report by David Yi-Yung Hsia, M.D., Julian L. Berman, M.D., and Herman M. Slatis, Ph.D., Chicago, in the current *Journal of the American Medical Association.*

Phenylketonuria is a disorder of the body's metabolism caused by a deficiency of an enzyme, phenylalanine hydroxylase. Because of the lack of the enzyme, phenylalanine, an amino acid essential to normal development, is not oxidized or used by the body. As a result, there is a gradual accumulation of phenylalanine from the diet to as much as 30 times the normal level in the blood after several weeks.

The biochemical abnormality and the mental retardation it causes can be treated successfully with a diet low in phenylalanine if it is started very early in infancy.

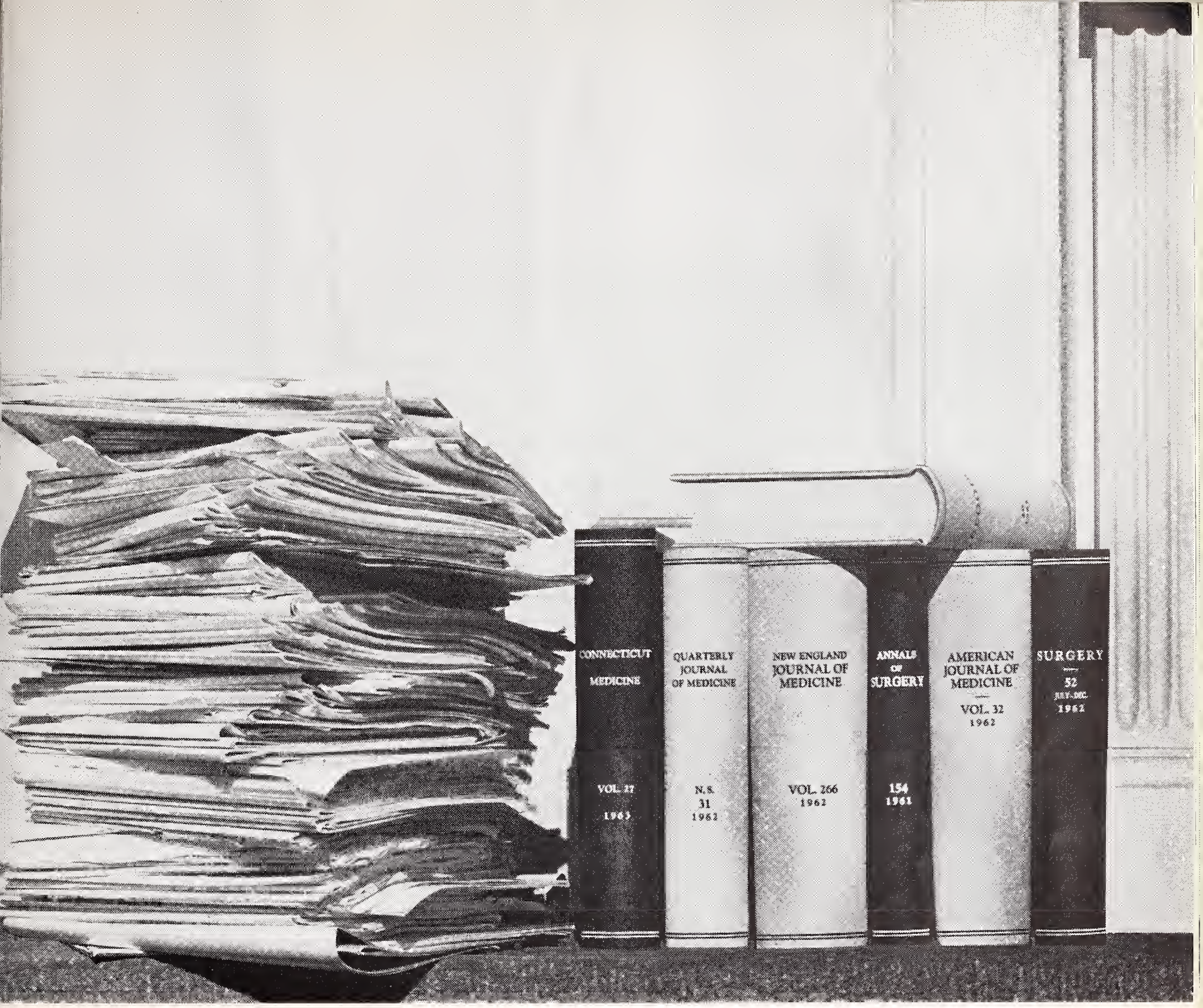
In the past few years, the testing of urine for phenylpyruvic acid has been used as a means of screening newborns for the disease.

Although this test is relatively simple, the Chicago researchers said, affected infants frequently do not show a positive tests until four to six weeks of age. By that time, they added, the babies will have been discharged from the hospital and complete follow-up is difficult.

The blood test method, which measures the level of phenylalanine in the blood, has been used on 4,000 newborn infants from five Chicago hospitals, the authors reported. The blood tests were performed at a central laboratory where as many as 150 samples could be processed by a technician in a day, they said.

"This method appears to combine a high probability of detecting affected infants with a small frequency of false positives," the researchers concluded.

Only 8 of the 4,000 infants showed a phenylalanine level above the upper limit of normality, they said.



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Unenforced Premarital Laws A Factor in Divorce and VD

The skirting of state laws which require premarital blood tests for syphilis and physical examinations is a factor in the nation's rising divorce rate and increased incidence of venereal disease, Dr. Sylvester W. Tryhall, a Detroit gynecologist, said in the current Journal of the American Medical Association.

The lack of complete premarital physical examinations, to determine disease, abnormalities, and general fitness for marriage, accounts in part for the "shocking" number of divorces, Dr. Trythall maintained.

In addition to detecting disease, a clear objective of the laws is to provide a marriage counseling opportunity to aid in establishing a harmonious family-situation, he pointed out.

If state laws were properly enforced, he added, blood tests could play "a decisive role" in early detection of venereal disease.

Nevertheless, he said, there have been moves to eliminate premarital blood tests in several states because of the high cost. The cost of detecting one infectious case of VD through premarital testing has ben estimated at from $2,000 in California to $30,000 in New York in past years.

Physicals and blood tests of both parties are required in 37 states, according to Dr. Trythall. States lacking both requirements are Indiana, Iowa, Mississippi, Nebraska, New Jersey, New Mexico, Oklahoma, Vermont, Maryland, Missouri, Nevada, South Carolina and Washington.

In a five-year survey of 2,500 private patients in Michigan, from 1955 to 1960. Dr. Trythall found that only 35 per cent of these women had received a complete physical.

'It is quite clear from these statistics that some examiners in Michigan are not complying with the law, no doubt in the majority of cases, because, neither the patient nor the examiner is aware that a physical examination for both premarital partners is a requirement," he commented.

The survey also showed that 20 per cent of these women obtained a "bootleg" certificate attesting to a blood test and physical which was not signed by a Doctor of Medicine or an osteopath as required by law.

Personal investigation revealed that certain Detroit laboratories were issuing "bootleg" certificates, Dr. Trythall said. In these laboratories, he explained, a single blood test was run in as short a time as 15 minutes, no physical examination was given, and no physician was present to sign the certificate in the presence of the applicant.

The public is in favor of the premarital laws even though they are not complying with them, according to the Detroit physician. The Michigan survey showed that 1,620 of 1,820 women, or 89 per cent, were in favor of the thorough physical examination required by law. Another survey of 500 Massachusetts wives showed that 80 per cent preferred a thorough premarital physical although only 20 per cent had received one, Dr. Trythall said, adding:

"Such strong expressions of favorable public opinion should serve as a mandate to the doctor . . . to oppose vigorously any legislation that would remove such statutes from the books. These statutes should be zealously upheld for their value as total public health measures."

Premarital laws should never be abolished, an accompanying Journal editorial said.

Sociologists and psychiatrists point to sexual irresponsibility, ignorance, and maladjustment as the major factors underlying the instability and unhappiness of many young married couples today, the editorial pointed out. Premarital laws provide the legal machinery to bring young people to the physician before marriage, at a time when ignorance and fear about sex can be evaluated most easily and, hopefully, overcome, it said.

Dr. Trythall said other reasons for the high divorce rate were that marriage counseling is not easily available, that 19 states have no waiting period for marriage, and that teen-age marriages are continuing to increase.

In a county area in southwest Michigan, he said, a recent survey showed that 250 of 265 teen-age marriages failed in the first five years.

Profitless Public Service Drugs

All of the ethical drug manufacturers have on their lists one or more drugs which are of use only to a limited few. Fortunately, there is no mass market for botulism antitoxin, antirabies serum, or actinomycin D, but these are on hand for use when needed. Such drugs are known to the trade as public service drugs and are provided after great cost of development at or below cost or free by the manufacturer who in many instances also pays the cost of emergency transportation. It is a great credit to the pharmaceutical industry that these products in limited demand are made available. There is more involved here than the loss-leader technic or a bid for prestige. Whatever the cynics may say, we believe that what is really involved is responsibilty. The companies feel it is their duty to serve the public and the medical profession in this way. This is something to remember during the present testing period for the industry. — Editorial in *New York State Journal of Medicine,* Dec. 15, 1963.

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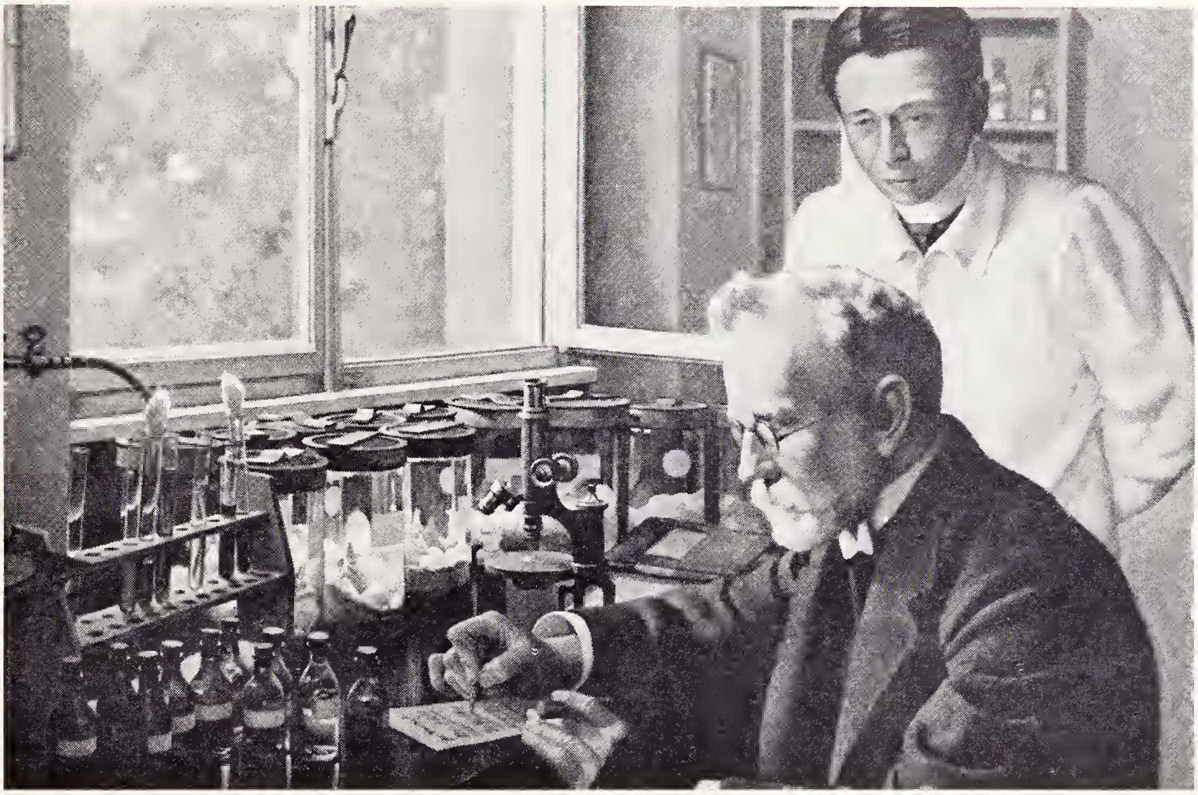

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EHRLICH: CHEMOTHERAPY IS LAUNCHED (See Page 561)

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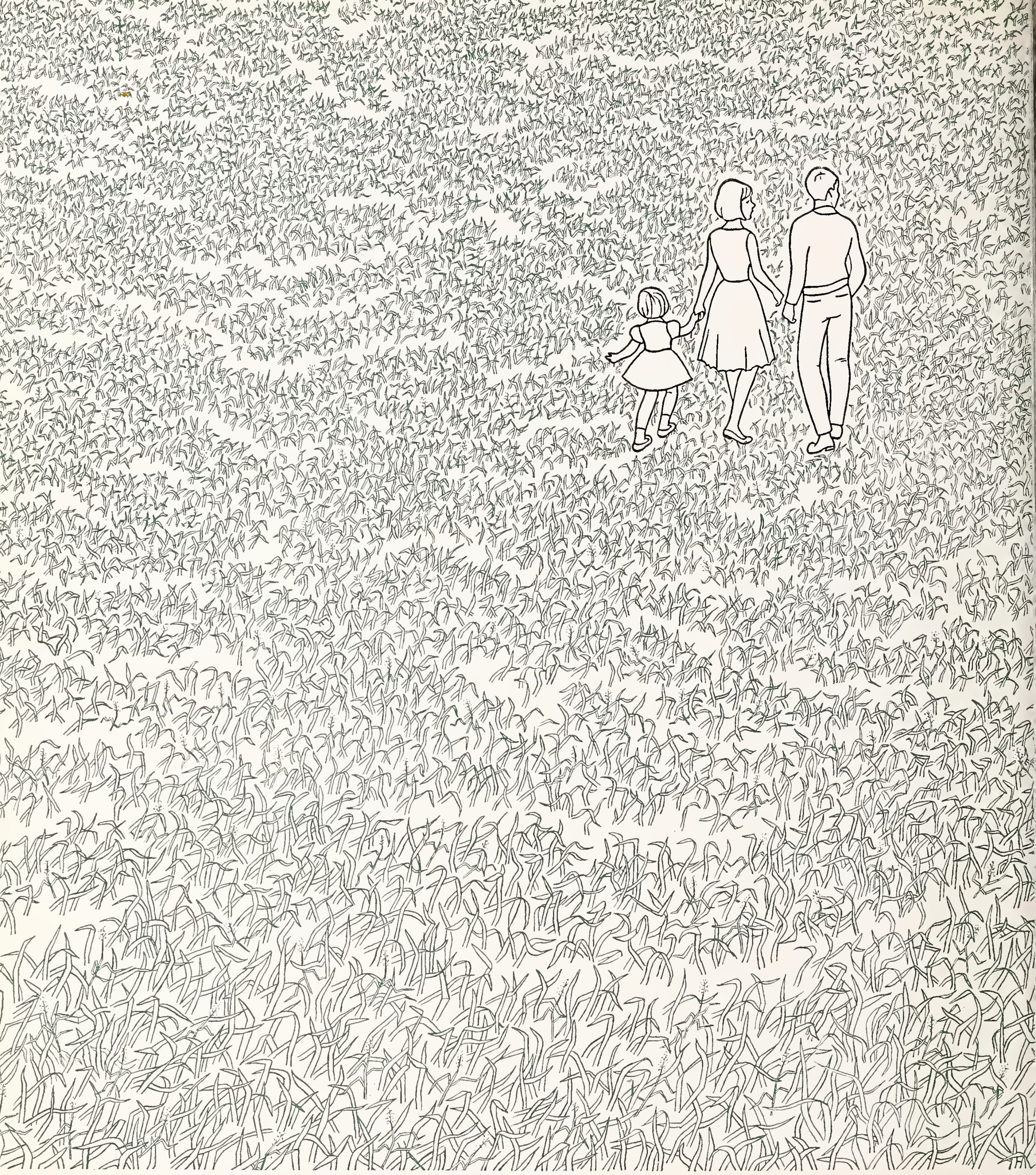

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Connecticut Medicine

editorials

The Doctor-Patient Rapport

Everyone agrees that there is much more in the healing art than the administration of medication. The road of pain and disability is easier to travel if the physician is able to relieve anxiety and instill confidence that his ministrations will succeed. The experienced physician has known for a long time that the morale of the patient can be an important factor in the battle for recovery. Hippocrates wrote long ago "where there is love of man there is also love of the art, for some patients, though conscious that their condition is perilous, recover health simply through the contentment with the goodness of the physician." In the word goodness, Hippocrates doubtless meant not only kindness but also ability to achieve successful results. In other words, there should be established a rapport between physician and patient to achieve the best result.

This truth seems so self-evident that when a sceptic raises the question of how do we know this; has such data ever been quantitated; we find surprisingly few authors who have systematically investigated this problem. Since rapport implies an interpersonal relation which is psychologic in nature, presumably we should seek such data in psychological investigations. An important preliminary approach to the value of rapport in therapy comes from the anesthetist.[1] In the past, anesthetists have interested themselves in various combinations of narcotics and hypnotics in order to prepare the patient emotionally for operations. The possibility that the personalities of the surgeon, anesthetist or ward personnel might have important effects in the preparation has been little explored. In fact there is not one study demonstrating the assumed effect of a doctor-patient relationship. In the preoperation state one has a fertile field for studying medication versus the physician-patient relationship.

Egbert, *et al*[1] have evaluated the psychologic condition of 449 private patients comparing the value of the preoperative visit of an anesthetist with the value of pentobarbital in 218 patients and then comparing the effects of two types of preoperative visits in 231 patients. Surprisingly, they found that the calming effect of pentobarbital is not statistically significant whereas the pre-operative visit definitely was. As was to be expected there were differences between different types of patients. Seventy-nine per cent of patients awaiting major surgery on the genitourinary tract were found to be anxious while of the remainder only 57 per cent were considered to be anxious. The most anxious patient was found to be the one awaiting an operation for possible cancer. Those patients who were calm the night before the operation remained calm before the operation and half became drowsy with pentobarbital. Of the anxious patients only 40 per cent became drowsy. The authors came to the conclusion that pre-anesthetic medication to allay anxiety does not achieve this desired result alone, and that other factors are important in the preoperative preparation of the patient especially psychologic preparation by a visit from the anesthetist.

When a patient consults a surgeon, his feelings about his illness may be modified by the surgeon. It is recognized that the patient's feelings about his illness seem to be due to his basic personality, the type of disease with which he is afflicted, and the organ involved. When the patient enters the hospital, then the care and attitude of the per-

THE COVER

EHRLICH: CHEMOTHERAPY IS LAUNCHED

In his crowded laboratory at Frankfurt's Institute of Experimental Therapy, German research scientist Paul Ehrlich (1854-1915) habitually scrawled work orders to associates with stubby colored pencils on "blocks" of note paper. Dr. Ehrlich and his Japanese assistant, Dr. Sahachiro Hata, announced Salvarsan (606) to the world in 1910 as a "chemical bullet" for treatment of syphilis. Dr. Ehrlich's success with chemical synthesis gave impetus to a new medical science, chemotherapy. Though his greatest achievements were in this field, Dr. Ehrlich contributed to many branches of medicine and shared in a 1908 Nobel Prize for his work on immunology.

sonnel on the wards may have an effect. Finally, in preparing for operation the anesthetist may influence the patient. It is therefore not surprising that any effect from pentobarbital may be overweighted by these powerful factors. Since anxiety is such a frequent and over-powering emotion in a person before his operation, it is to be expected that emotionally supporting pre-operative visits would give better results than just medication. This in fact emerged from the statistical study of Egbert *et al.,* that the differences in the behavior of the anesthetist influence the patient. The patients gained confidence and were calmed even though the anesthetist spent but five to ten minutes with them.

At first sight it would seem surprising that an anesthetist in such a short interview the night before operation would be able to exert a psychologic effect demonstrable the following day. The authors doubt that merely learning about his anesthesia could be an adequate explanation. A better explanation is provided by Janis[2] who found that persons facing a frightening situation became anxious and looked for emotional support. These patients found the best emotional satisfaction by obtaining a realistic view of the crises facing them. Some patients actively seek information while others attempt to deny the existence of the impending danger. One needn't be much of a profound student of human nature to be able quickly to discern between the two types. Nevertheless, an authority supposedly able to modify danger becomes invested with strong emotional significance and the statements made by this authority assume greater importance than would ordinarily be expected. Eckenhoff and Helrich[3] believe that "the anesthetist should never underestimate the pre-anesthetic visit. . . . Preoperative medication should be tailored to meet the needs of the patient. . . . Each patient must be considered individually."

It would be important to know in general, the degree of rapport that physicians establish with their patients. No data on this subject is available, though much moralizing and beliefs are confidently expressed on this subject. We do know however from Sheffer and Greifenstein's studies about anesthetists that until the present they have established little rapport with their patients.[4] The anesthetists were thought of as skillful doctors who lacked emotional impact. Many patients were actively curious about the anesthetic and wondered who their anesthetist was. Nevertheless, the patients interest in knowing about anesthesia is not what they needed. They were faced with a crisis and wanted emotional support. From our knowledge gained from the anesthesiologist we begin to see a scientific basis over and aside from humanitarian and moral aspects for the importance of the physician-patient rapport. It yields results, in allaying anxiety.

We are deluged with such phrases as "there is a tendency to devote too much attention to medical science and too little to the art of medicine." "More is required than superficial words of encouragement." "The sentiment expressed should come from the heart." "Affection can warm the coldest temperament and soften the hardest heart."[5] It is time we begin to ascribe some concrete meaning to what the physician turned philosopher demands of us in the successful pursuit of the art of medicine. We have believed that allaying anxiety helps recovery from disease but we did not know this quantitatively. We know, now, it relieves patients from suffering. This is a worthy purpose even if it does not cure. But this is an approach based upon psychological knowledge. Instead of talking about it in high phrases with humanitarian import, let's find out. The anesthesiologists have pointed the way.

L.H.N.

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Science Tools: 7. The Lymphocyte And Histocompatibility

We are entering into an era of tissue transplantation. Kidneys have been successfully transplanted in man and hearts in dogs. The big difficulty of course is the existence of genetic dissimilarity between donor and recipient. In blood transfusion we have a typing method which makes it easy to choose compatible blood for the recipient. It would be highly desirable in order to evaluate potential donors for tissue and organ transplants, if a test were available, that would help to establish the compatibility of donor and recipient in vitro. If such a test were available it could prove useful in tissue typing, thereby greatly reducing the rejection rate in tissue transplants. It is genetic similarity between the donor and recipient of a transplanted tissue which appears to be the major factor responsible for the success of a transplant.

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We know that in skin transplantation, if the donor and recipient are genetically identical, the graft will take. In humans the chance for success with kidney transplantation increases if the donor and recipient are blood relatives. With identical twins there is uniform immunological success. Because of these facts much work has been devoted in recent years to the problem of selecting suitable donors for tissue transplantation. One method for testing histocompatibility has been by placing successive skin grafts from prospective donor and recipient pairs on a third unrelated individual. Another method using human beings to test differences in immunological constitution between donor and recipient is that of Brent and Medawar. Lymphocytes of the recipient are injected intradermally in a series of potential donors. The intensity of the delayed type response to the lymphocyte is then correlated with the rapidity of breakdown of subsequent grafts from the donors to the recipient. If the donor reacts severely to the recipient's lymphocytes, the survival time of the donor graft is short. On the other hand if the donor accepts the recipient's lymphocytes without reaction, then the donor graft will survive.

The methods mentioned above are laborious. If one could test the compatibility of donor and recipient in vitro we will have gone a long way towards tissue typing and genetic analysis. Bach and Hirschhorn[1] have just published a method which seems to have opened up the whole field of genetic analysis and understanding of histocompatibility. They have shown that lymphocytes from two unrelated individuals when cultured together in the same tube undergo morphological transformation to large cells and divide. Both the number of large cells and mitoses can be estimated quantitatively. Furthermore, there is a correlation between the degree of this response and the histocompatibility of the donor and recipient. A low number of large cells and few mitoses means the donor and recipient are histocompatible.

In this manner large numbers of intra and interfamily studies can be done that will give us an understanding of genetic similarity and dissimilarity between individuals. The method might also make it possible to set up a panel of white cell donors similar to the panel of red cell donors now in existence. This could be used for typing a recipient and all potential donors.

Up to the present time this technique of lymphocyte culture offers a new approach to the problem of donor and recipient typing for renal homotransplantation. It also provides a way of evaluating the degree of immunologic suppression affected by cytotoxic agents. Lymphocyte matching in vitro was performed for two female patients with terminal renal disease[2] as a guide to the selection of renal homograft donors from members of the same family. One was found compatible with the father, the other with the mother. Four months have elapsed since transplantation in one and three months in the other and both have shown only minimal evidence of graft rejection.

Use of this technique should allow further insight into the problem of histocompatibility and the nature of drug-induced suppression of the immune response.

L.H.N.

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Electrical Conversion Of Cardiac Arrhythmias

It has been known since the turn of the century that both alternating current (AC) and direct current (DC) countershock could arrest ventricular fibrillation in an exposed dog heart. However, it is only recently that successful defibrillation of the ventricles in human beings could be achieved with AC applied through a closed chest. More recently closed chest AC countershock has been successfully employed in human beings with arrhthmias other than ventricular fibrillation such as supra ventricular tachycardia, ventricular tachycardia, atrial flutter and atrial fibrillation.[1, 2]

Within the last two years Lown[3, 4] and his associates have advocated the use of DC countershock as a replacement for AC countershock in the above arrhythmias on the basis of greater safety and efficiency. They demonstrated that the short duration of the direct current shock (1.25 to 2.5 msec.) as compared to 150 msec. for a standard AC defibrillation, combined with electronic triggering so that the shock is initiated 20 msec. after the R wave of the electrocardiogram, avoids the vulnerable period of both the atrium and the ventricle. This lessens the chance of producing either atrial or ventricular fibrillation by AC countershock which may occur because of the random application of the impulses by this method.

Kuhn[5] has studied this problem in ten dogs with repeated DC shocks over an interval of 45 minutes. He noted that AC as compared to DC countershock produced a higher incidence of episodes of ventricular fibrillation (17 vs. 1.9 per cent), of atrial fibrillation (66% vs. 0), of myocardial infarction (90% as compared to 33%) and death (50% as compared to 0). Ventricular premature systales occurred with equal frequency in the two groups and complicating ventricular tachycardia was slightly more frequent with DC shock (29 vs. 17%). Moreover, of ten dogs with ventricular fibrillation, AC was effective in defibrillation of 9, and in one animal AC shocks up to 750 watts were ineffective in defibrillation although this animal was defibrillated with one DC discharge.

There is other evidence which favors the use of DC countershock in ventricular fibrillation and other cardiac arrhythmias as compared to AC countershock. It comes from studies in hypothermic dogs and from pathologic studies. In the former, DC countershock was successful in each instance in which AC countershock did not succeed at body temperatures of 20-30° C. In pathologic studies, there was less histologic evidence of myocardial damage after DC countershock than after AC.

The above objections to the use of AC countershock, based on previously mentioned experimental data, and the availability of Lown's instrument for delivering programmed DC countershock, has advanced the clinical use of DC countershock since its initial introduction. In the last two years great attention has been focused upon the use of DC shock for the conversion of a variety of acute and chronic arrhythmias. Lown and his associates have utilized programmed DC countershock in the treatment of a variety of acute and chronic supraventricular arrythmias and in ventricular tachycardia in closed chest human subjects. The impulse as noted above is delivered 20 msec. after the R wave peak. This more recently reported experience is with over 100 patients mainly with atrial fibrillation. Successful conversion has been accomplished generally with one or two shocks in over 90 per cent with no reported complications from the procedure.

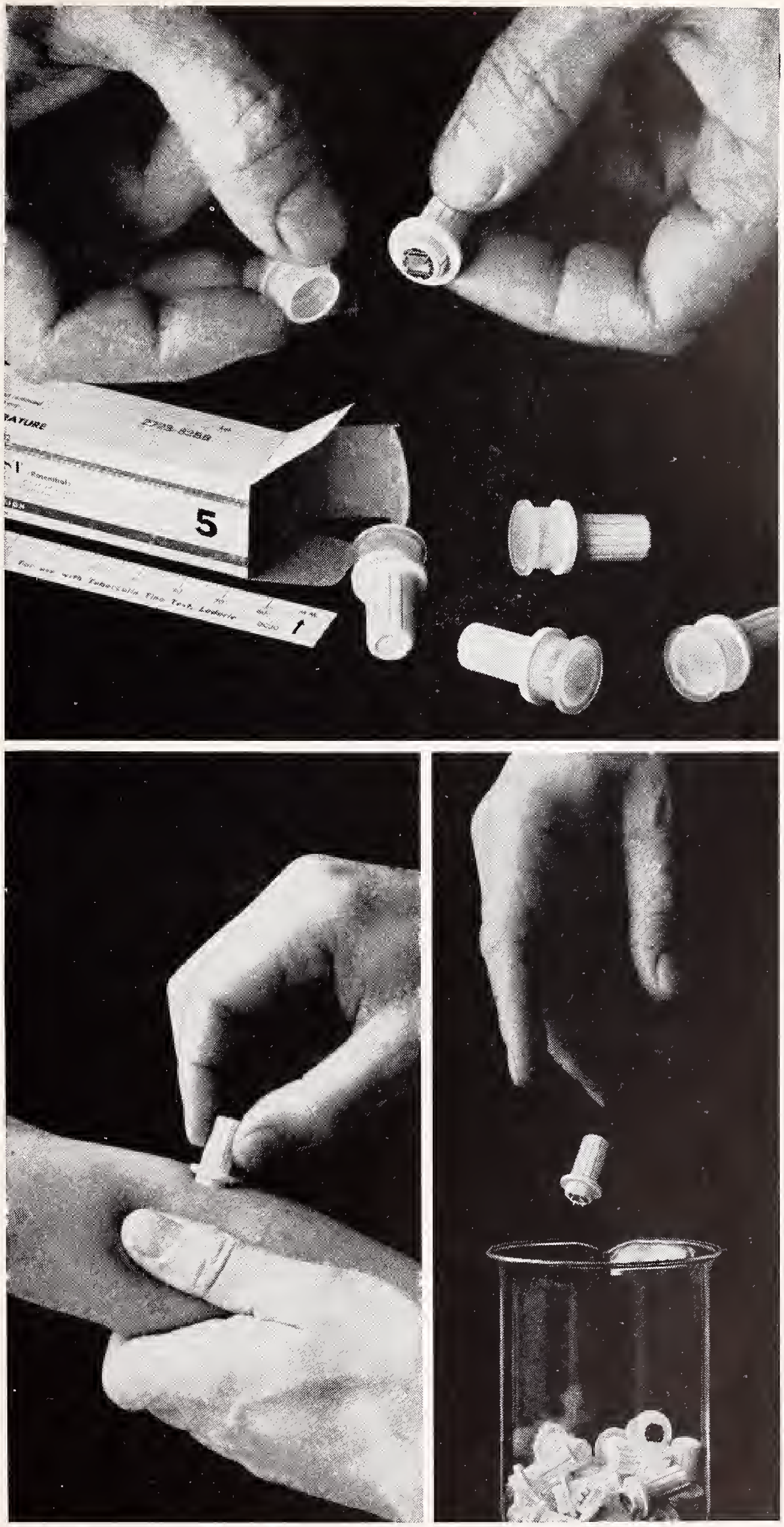
Other published experiences with this technique has in general confirmed Lown's observations, even to its trial without general anesthesia. There are undoubtedly many more instances of the successful use of D.C. countershock in various centers throughout the country which are yet to be published. The indications are that Lown's impressive results are being confirmed by other investigators. It has been recommended that anticoagulants be used as well as prior administration of quinidine in atrial fibrillation due to rheumatic heart disease. Up to the present time such suppressive therapy has not prevented a focus from assuming a role of pacemaker.

It is apparent that DC countershock as it is presently used is generally sufficient and effective. Although, even with "properly timed" DC countershock ventricular fibrillation can occur, in the one case in which it was reported, it was easily reverted with a second shock. Taking into consideration those experiences in which AC countershock failed to revert ventricular fibrillation while DC succeeded, it is understandable why the bulk of future observations with these arrhythmias are likely to be with DC countershock.

It is already apparent that transthoracic electrical conversion of arrhythmias represent a very useful clinical method in a variety of situations. First is in the conversion of arrhythmias that do not respond to appropriae drug therapy or in which the amount of drug that must be used for conversion proves hazardous. Then there are situations in which undue delay may be encountered in administering the drug, a delay that might threaten the life of the patient. Finally, when precise electrocardiographic interpretation of the arrhymthmia is not feasable so that it may be difficult to decide on an appropriate drug therapy.

In acute arrhythmias which seriously compromise cardiac output, countershock may result in prompt dramatic and permanent return to normal sinus rhythm with rapid improvement in the patient's clinical state. However, it is not that easy in chronic atrial arrythmias such as atrial fibrillation due to rheumatic heart disease. In this arrhythmia there is as yet no evidence and there is no reason to believe that electrical conversion to sinus rhythm will be any more permanent than is drug conversion provided of course that similar maintenance schedules of quinidine are used. At the moment general anesthesia seems to be required in most instances. However, under certain circumstances, especially when no more than 100 watt seconds or less is required, then the procedure can be performed without anesthesia. Any refinement in the procedure that may achieve defibrillation with a diminished voltage will of course permit more procedures to be performed without anesthesia. In fact, there is already some indication that an anterior-posterior placement of electrodes may permit success with a dimished voltage.

In many instances it is conceivable that the greater simplicity of countershock and the need for less precise electrocardiographic interpretation of complicated arrhythmias may cause this method to be used without any attempt at drug therapy, even though anesthesia may be necessary. In fact, there is already some tendency in certain medical centers to adopt this view at present. However, more experience will be necessary before there is



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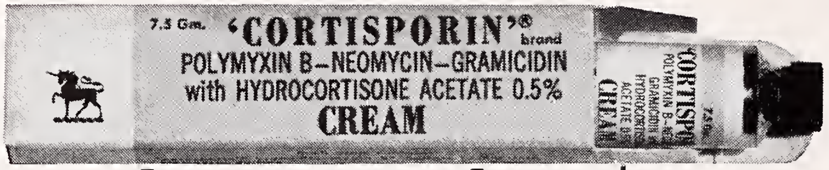
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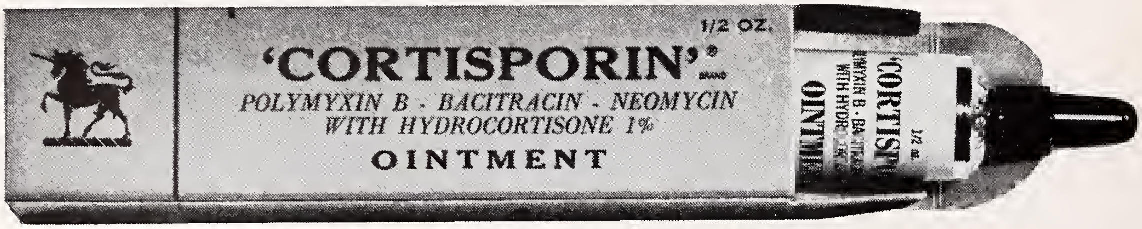

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general acceptance and application of the method without a preceding use of drugs.

L.H.N.

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Spacing Of Children

The spacing of children certainly has merit. It can help a mother get used to the duties of motherhood in a more balanced way. It can aid her in taking on responsibilities with a greater reserve of kindness and generosity and at the same time with more physical strength. These matters are aside from the question of a mother being over burdened with economic requirements of feeding, clothing, and educating a large number of children and the adverse effects such problems might have on the personality development of both parents and children. But to successfully achieve voluntary spacing of children is not an easy matter even though there are medical eugenic, economic and social indications.

In 1951 Pope Pius XII stated "We have affirmed the legitimacy as well as the . . . limits of a regulation of offspring which . . . is compatible with the law of God. One can even hope . . . that medical science will proceed in giving this licit method a sufficiently secure foundation, and the most recent information appears to confirm such a hope."[1] The licit method referred by Pope Pius XII was described by him[2] as "the taking advantage of natural temporary sterility." What then are the probabilities of success in the spacing of children for normally fertile couples particularly those who choose to use the natural methods only.

Agino and Kraus[3] have each suggested that fertilization can occur only during certain unsafe days in the middle of each cycle, but that it requires thirteen cycles of observation before you can establish reasonably "unsafe" days an almost impossible task without becoming pregnant. deBethune[4] points out that many couples who use the rhythm method cannot achieve thirteen cycles of observation without encountering a pregnancy first. To them the potentially attainable security after prolonged observation becomes of academic interest only. The very best results by the rhythm method alone results in the spacing of births of only between one and two years. deBethune points out further that the menstrual pattern changes after childbirth and can become increasingly erratic after repeated pregnancies. For this reason the mother of many children who is most in need of a reliable method of child spacing is the very one for whom the calendar method is likely to fail. Furthermore with the menstrual cycle in general as with the weather, past performance is no guarantee of what is going to happen. No matter how long or how regular the cycle has been the Ogina-Kraus method is never proof against the vagaries of an erratic fluctuation in the current cycle.

If one wished to space children three to four years apart the use of contraceptives could raise the factor of security against pregnancy, but here again the security factor drops with an increase in the frequency of coitus and more consistently with any relaxation of vigilance. However, to space children four years apart by the rhythm method alone is not attainable at all. Even if one wishes to space births eighteen months apart by the rhythm method, the odds against a birth in this period are 3:2 but for a spacing of twenty-four months, the odds now become 4:3 in favor of at least one birth in the given period.

There are many national or ethnic groups whose members on religious, moral, cultural or economic grounds find contraception unacceptable, too expensive, or impossible to practice. The needs of these people make the appeal of Pope Pius XII for more secure methods based on "taking advantage of natural temporary sterility" more urgent now than when it was uttered by that great Pontiff in 1951. And this appeal was echoed by Cardinal Suenens[7] at the Brussels Health Congress in 1958. The taking advantage of natural temporary sterility has theretofore meant use of methods based on the natural regular or irregular rhythmic cycle of fertility and sterility of the wife. The crux of the method resides in finding as accurately as possible the exact timing of ovulation.

It is now patently clear that whether this method is to be determined by an extrapolation to the current cycle of the patterns of previous cycles or whether by the Ogino-Knaus method or from the record of temperature charts, the success of the rhythm method in spacing children is extremely limited, even if the fertile period is as brief as twelve hours. deBethune shows that a couple who desire a two year spacing are limited statistically to two acts of coitus per cycle and couples who desire a four year spacing are limited to a maximum of one act of coitus per cycle. It is not surprising that the rhythm method has become a source of mental torture to many couples.

What then is needed to make spacing of children more secure? We need an accurate ovulation prediction test which can give a dependable signal three days in advance of ovulation.[5] An alternative would be an accurate method of precipitating the occurrence of a late ovulation on a controlled day. This has recently been done by hormone injections but only on an experimental basis.[5] The moral objections that are now raised against suppression of ovulation as a "direct sterilization" do not apply to control of the timing of ovulation. If an ovulant pill were to be developed that could restrict ovulation to a period during the menstrual cycle, this could solve the problem of making the rhythm method reliable for those couples who are motivated to use it.

Up to this time we have spoken of natural temporary sterility in the female. But a man's fertility also needs elucidation. Male fertility has been found to undergo variations also, in a purely natural way in relation to working, exercise, dressing and bathing.[6] If the monthly security factor against pregnancy is to be raised by employing methods based on natural temporary sterility in accordance with Pius XII expressed wish, to a level such that effective child spacing is no longer a statistical impossibility for many couples, then we must learn and master the natural variations in the fertility and sterility of both man and woman. Then mankind can in Pius XII own words take advantage of them.

L.H.N.

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Nature and Nurture

Traditionally many behavioral scientists have assumed that individuals start life uniformly alike and that the individual differences which we see result only from different experiences. Long ago, Watson concluded that we had no real evidence for the inheritance of traits and insisted that hereditary structure though different from one individual to another "lies ready to be shaped in a thousand different ways."[1] Now with the tremendous increase in our knowledge of heredity, the behaviorists still assume that all genetic combinations are usually plastic and respond in a like fashion to environmental influences. This over emphasis on environment found its great protagonists in politics too in the Soviet Union where genetics for a time were taboo and Lysenkoism was universal doctrine. It should have been common knowledge that within each population, the variation pattern for most traits will be conditioned by the gene pool and this will differ among populations. This genetic basis for individual differences also found its protagonists in the murder-producing pseudogenetics of Hitler and other purveyors of race prejudice.

We are now in a more fruitful period, one in which we are learning how genetic factors contribute to individual differences and also how experimental factors do also. With experimental analysis we are learning information about genes and chromosomes and how they act. This has opened a way to understanding molecular and ultimately submolecular mechanisms and to following metabolic pathways between genes and the phenotype. We are rapidly learning the facts about behavior genetics of many organisms. For example, there exist individual differences in rats in their ability to learn. Some are "maize bright," others "maize-dull." By selective inbreeding, strains of rats of each variety can be produced. Furthermore, one can select for differences in emotional response. By appropriate genetic crosses it can be shown that such behavioral differences as alcoholic preferences, hoarding, mating competition, as well as various learning measures have genetic correlates.[2]

Rothenbuhler[3] found that resistance to foulbrood disease (a bacterial infection of the larva of the honey bee) depends on homozygosity of the worker bees for recessive alleles of at least two genes, one which enables them to uncap compartments containing infected larvae and another which enables them to remove those larvae from the hive. Hirsch[2] found genes influencing the response to gravity in Drosophila. An existing development is Hyden and Eghyáze's[4] measurement of changes with learning in a certain repressed DNA. The idea is that electrical disturbance of the nerve impulse releases

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a depressed region of chromosomal DNA. This DNA henceforth produces on demand its characteristic RNA to produce a protein which facilitates forward transmission of the particular pattern of electrical impulse that just released the RNA. Is this genetic feature of individual performance the explanation of the universal feature of improvement with practice? If this is so, then learning and memory mechanisms are encoded in the chromosomal DNA of the genotype at meiosis and fertilization and propagated directly into the individual.

The study of man has moved beyond the stage of wondering whether we can find a hereditability for this or that behavior. Hundreds of genetic traits have been uncovered, not only of individual gene mutations like that giving rise to phenylpyruvic oligophrenia, but to whole chromosome abnormalities like mongolism. Human populations are dimorphic for taste sensitivity to certain bitter compounds. Some individuals have an enzyme in saliva that quickly destroys thiourea. These are "non-tasters." A correlation seems to exist between taste sensitivity and dislike of food. The more sensitive tasters, those who have no enzyme to oxidize thiourea, find more food objectionable. This genetically controlled tasting phenomenon has wide ramifications. Parents as well as children with goiter seem to have a high incidence of nontasters. Likewise do parents of mongol infants.[5]

We thus see that genetics can and does explain individual uniqueness. Even in populations that belong to the same species and have the same genes, the relative frequency of different alleles of genes and the gene pools are almost certain to differ. Mutations and recombinations will occur at different places at different times and with different frequencies. The real questions to ask in the present state of our knowledge is not whether individuals and populations are different but rather in what ways they differ. Organisms which we study are intrinsically variable before they undergo differentiating experiences through the mechanisms of mutation, recombination and meiosis. The traits of individuals which we seek to study and understand are unlimited. They are the developmental results of thousands of genes, most of which because of crossing over sooner or later undergo independent assortment.

Having said this about genetics, it is important to emphasize that environment is no less important. The growth and development of a responsible and effective citizen requires prolonged socialization and is highly dependent upon how this is carried out. A genotype must have an environment in which to develop a phenotype. Nevertheless, the same genotype can produce quite different phenotypes depending on the environment in which it may develop. Parents and teachers are well aware that a given environment can nurture quite different phenotypes depending on the genotypes which may develop there. One method of instruction which may be admirably suited for one child may be worthless for another who nevertheless can learn by a different method.

So while environment makes an undeniably important contribution to the particular value obtained from measuring a specific individual, the consideration of the environment should not change our general picture of the structure of an individual or a population. Without an appreciation of the genotypic structure of populations we have no way for distinguishing individual differences which can be attributed to differences in previous history from those which are not. Neither have we a basis for understanding any differences between individuals where there is a common history. If we recognize that the effects of experience are conditioned by the genotype, then the violent controversy between nature and nurture appears in a totally different perspective. The outlook for understanding the physical basis of behavior has never been more promising.

L.H.N.

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The Lymphatic System

1. Cardiac Lymphatics And Obscure Heart Disease

A closed cardio-vascular system required the development of an effective lymphatic system to clear the tissue spaces of protein, fluid and electrolytes which escape from the blood vessels in considerable amounts. In fish, amphibia and reptiles, the lymphatics have no valves and the lymph is propelled by lymph hearts. In birds these lymph hearts disappear after embryonic life. It is in mammals that the lymphatic system achieves its most complex organization. The system has been known for a long time, being traced back to Rudbeck in 1653.[1] As far as the lymphatics of the heart is concerned Kampmeier[2] had already in 1928 described their development in the fetus of the human heart. It is therefore surprising how little it is appreciated that a well defined lymphatic system exists in the heart and how little thinking has been done regarding the role of this system in heart disease.

It has been recognized for a long time that chronic impairment of lymph flow from a region of the body results in tissue fibrosis and predisposes to infection and inflammation. Why then has not this thought been carried over to consider what conditions in the heart might result when chronic obstruction of the cardiac lymph drainage takes place? One reason was the great technical difficulties involved in their study. But another and perhaps more important one was the absence of a hypothesis to relate the cardiac lymphatics to the many known diseases of the heart. Once the idea occurred to Miller that cardiac lymphatics can be implicated in a variety of clinical types of heart disease, it was not difficult to overcome the technical problems and create a model system of study by causing obstruction of the cardiac lymphatic drainage system in dogs. After four years of working on this problem Miller has recently reported his results.[3]

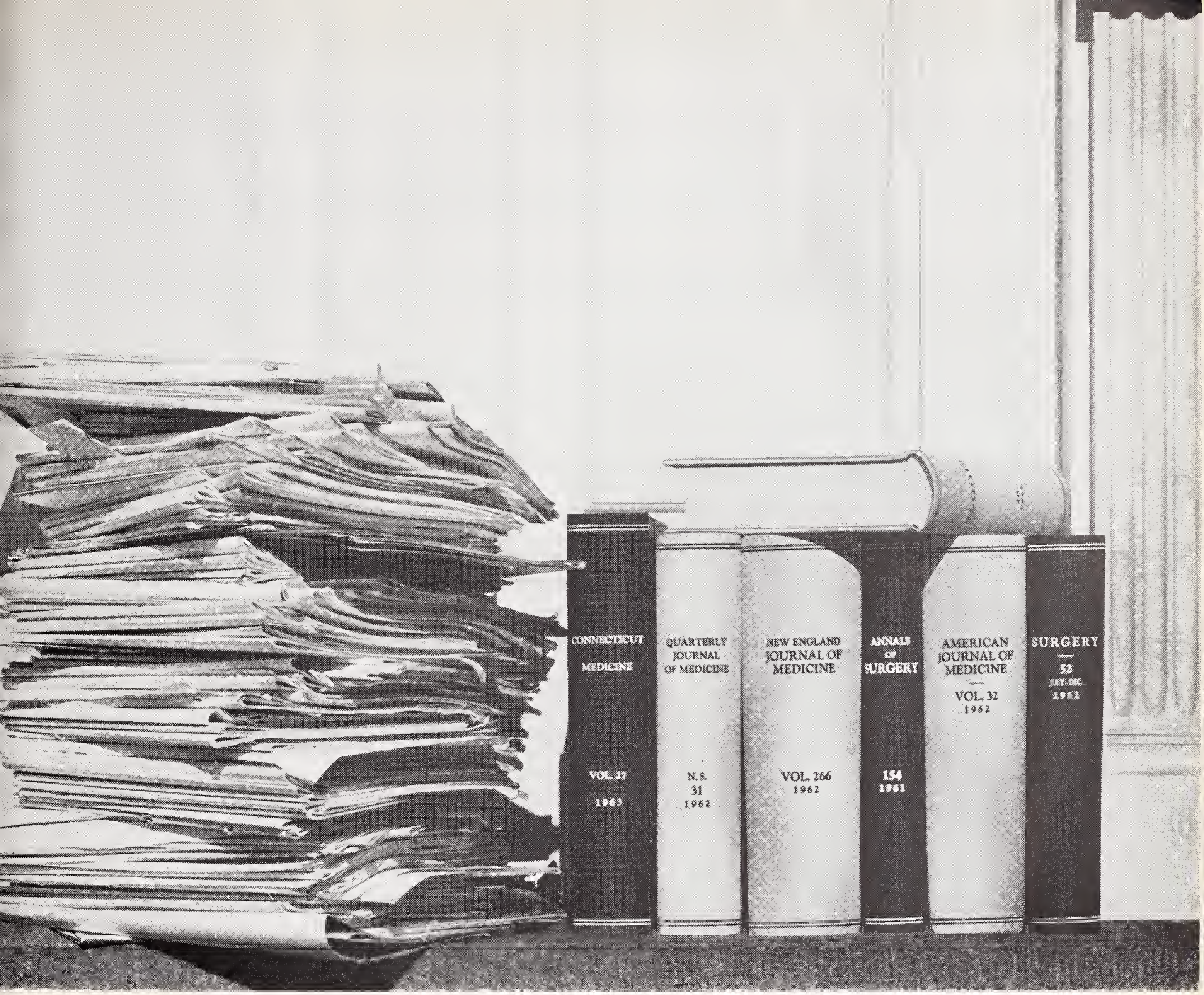
First it became easy to show that the anatomy of the cardiac lymphatics as described by Patek[4] is correct. There is a substantial subendocardial and sub-epicardial plexus of lymphatics. The subendocardial plexus drains into the myocardial plexus. From here a large series of interconnected capillaries drains into an extensive sub-epicardial system which covers the surfaces of both ventricles. The channels of the sub-epicardium then unite to form drainage lymphatics which accompany cardiac blood vessels. These drainage lymphatics which contain valves eventually join to form a single trunk which leaves the heart at the base of the pulmonary artery. They then invariably enter the pretracheal node in the area of the descending limb of the arch of the aorta. From here they go to the cardiac lymph node which lies between the superior vena cava and the innominate artery finally entering the right lymphatic duct. Besides this clearly defined system, Miller found lymphatic plexuses on the atrial surface of the mitral valve leaflet and also on tricuspid valve leaflets.

Thus the mammalian heart has an extensive lymphatic system. It is not surprising that this is so if one remembers the physiology of this system. Wherever there is interstitial fluid it must be drained off. As fluid leaks from the arterial ends of the capillaries into the interstitial spaces only very small quantities of protein can accompany it but then as the fluid is reabsorbed at the venous end of the capillary most of the protein is left behind, unless it gained access to the lymphatics. By washing the proteins out through the lymphatics the tissue spaces automatically returns the protein concentration again to normal levels.[8] If it were not for this continual removal of proteins, the dynamics of the capillaries would become so abnormal within only a few hours that life could no longer continue. In short the lymphatic system represents an accessory route by which fluids can flow from the interstitial spaces back into the blood. In fact, the lymph draining any area is a good indicator of the regional interstitial environment. This idea has not been sufficiently explored certainly as regards cardiac metabolism although renal lymph has been studied by Lever and Peart.[5]

The question of course, remains as to what happens when there is interference with lymph flow in the heart. In other parts of the body there is abundant evidence that interference with lymph flow predisposes to infection, inflammation and the laying down of fibrous tissue in the affected part. Does this also occur in the heart? Rusznyak[6] found cardiac interstitial edema when the lymphatics were impaired. He found disseminated focal necrosis in the myocardium, hemorrhages, and significant electrocardiographic changes. Elevation of serum transaminase indicative of cellular injury has also been described. Miller found ventricular subendocardial hemorrhages, gross and microscopic thickening of the ventricular endocardium due to increased elastic and fibrous connective tissue which appeared after eight days. He found in six dogs severe spontaneous ventricular endocardial fibroelastosis and by chance demonstrated significant decrease in lymph flow in two before death.

When he injected autologous blood into the ventricular myocardium of dogs in whom he had produced chronic impairment of cardiac lymph flow, he observed development of substantial focal necrosis and a persistent inflammatory reaction not found in control dogs. Furthermore, if he injected staphylococci in his experimental animals, over one-third developed bacterial endocarditis while control dogs remained free. Not only in dogs but also in a case of severe chronic myocarditis in man Miller observed a marked case of fibroelastosis associated with dilated lymphatics in the subendocardium and myocardium.

From Miller's studies there emerge two possible directions for development of disease when cardiac lymphatics are obstructed. Subendocardial hemorrhages may heal with predominent fibrosis, or late lesions may be predominantly increased elastic tissue, when there have been few or no early subendo-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cardial hemorrhages. It is certain that in man there are instances of impaired lymphatic return, particularly in myocarditis. In Chagas myocarditis, endocardial fibrosis is relatively common. Endomyocardial fibrosis is seen frequently in Africa where parasitic infestation of the heart is common.

If in man, impairment of cardiac lymph flow were to occur in utero, then we might expect the laying down of endocardial elastic tissue. If the lymph flow obstruction occurs in the adult from whatever cause, it might result primarily in endocardial fibrosis. Interference with the lymph drainage of a heart valve by rheumatic valvulitis might be a factor in the subsequent gradual fibrosis. Moreover interference in lymph flow might play a role in the subsequent predisposition to inflammation and infection. It is interesting that the mitral valve in dogs becomes more susceptible to staphylococcus infection, because rheumatic valves also are more susceptible to bacterial infection and this on the atrial surface just as happens in dogs.

There are many other questions concerning the possible role of the lymphatics of the heart. To what extent may the size of hemorrhagic myocardial infarction and the extent of the scar formation, be related to the efficacy of the lymphatic system in removing the products of tissue destruction? Can enlargement of the aortic arch or innominate artery so compress the cardiac lymphatic return as to interfere with myocardial function? In chronic myocarditis interference with cardiac lymphatic drainage may be a determinant of the degree of resulting muscle fibrosis. Perhaps injury to the lymphatics in acute myocarditis may be a determining factor in perpetuating the chronic inflammatory process. Then there is the speculation by Rusznyak[6] that impairment of lymph flow from the heart in congestive failure may aggravate myocardial lesions and further enhance heart failure.

We are indebted to Miller for his productive studies which will certainly serve as a guide to future work. It is apparent from the studies to date, that the cardiac lymphatic system is important in cardiac physiology and pathology and thinking of this system has added a new dimension in how we will think of heart disease. It will become easier to investigate the obscure forms of cardiomyopathies[9] with the lymphatic system as a guide-post.

L.H.N.

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Five New Viral Exanthems

Skin manifestation of viral exanthems have always been of interest to clinicians because of their frequency (childhood exanthems and their manifest visibility). The specific eruptions of the classical viral exanthems rubeola, rubella, varicella, herpes simplex and herpes zoster have made bedside diagnosis of these illnesses easy, and have enabled predictions as to the probable course in these patients. Now that it is possible to grow the causative agents in tissue culture we have been enabled to study the incubation period and clinical course in relation to virus multiplication in the body. There has thus opened up the possibility of vaccine prophylaxis and specific chemotherapy.

During the summer and fall each year many children and some adults are seen by physicians with rashes that are clearly not one of the well known eruptions. With blood cultures, tissue cultures, cultures from vesicles, the offending viruses have been isolated and propagated, so that the etiologic agent in these exanthems has come under close study. At the present time 5 new viral eruptions, not previously recognized are fairly well characterized.[1] Aside from laboratory studies, even clinically it is possible to arrive at a differential diagnosis of these exanthems. First from the distribution and appearance of skin lesions associated with physical findings and laboratory tests including stained smears of lesions. Second, an etiologic history can contribute significant information such as multiple illnesses in the family, recent travel or other exposure and a knowledge of epidemics of viral diseases in the community. In fact this often is as essential for accurate diagnosis as is the nature of the eruption itself.

Rickettseal exanthems are similar in many respects to viral infections, but the five viral infections clearly delineated by Lerner[1, 4] are of special significance in our communities. These are the Boston exanthems,[2] Coxsackie B5 infection, Coxsackie A9 infection, Vesicular Stomatitis with exanthems (Handfoot and mouth disease)[6] and ECHO9 disease associated with specific ECHO virus infections. These illnesses have been found throughout the United States, Canada, Europe and South Africa. In fact to discover these exanthems it needs only an adequately prepared physician.

In a study at the Boston City Hospital during three summers 1959-1962, 146 such cases were recognized and studied.[1] They began to appear in June and occurred regularly through September but with a peak in August. On an average three such exanthems were seen each week of study, more than half of which, were seen in children under 2. The illnesses were brief usually associated with fever. The incubation period was 2-8 days and often several cases appeared simultaneously in a single family. The rash was present for as brief a period as 24 hours and for as long as 5 days. The illness was moderate, the average temperature was 101-103F and persisted for 1-4 days. Although the viruses concerned were enteric viruses, nausea, vomiting and diarrhoea were not increased. Adenopathy was not marked. The rashes were most frequent in younger patients, but a general trend towards more severe illness was found in older persons with or without rash.[1]

Virus was isolated from blood, pharynx, serum or cerebrospinal fluid at a time when the patient was still well. The blood contained virus in high con centration during the incubation period and it was during this period that seeding in distal foci took place such as skin and the meninges. Obviously it is during this period that an agent like hyperimmune gammaglobulin could neutralize the circulating virus and prevent the manifest disease. The first of the new exanthems was recognized by Neva et al[2] during an outbreak in Boston in 1951 and again in Pittsburgh in 1954.[3] It was called the Boston exanthem and was caused by ECHO 16 infection. Often there was a mild sore throat with punched out ulcers of the soft palate and tonsillar pillars not unlike those of herpangina. The rash appeared as the fever declined. It was a pink or salmon colored macular to maculopapular eruption, consisting of lesions that were usually discreet 0.5 to 1.5 cm. in diameter appearing first on the face or upper chest. If the rash became generalized the palms and soles were also involved. Illnesses associated with Coxsackie B5 infections could not be distinguished from the Boston exanthem and resembled roseola infantum. Perhaps viruses are closely related and produce the same clinical picture.

Two other exanthems are associated with viral causes, coxsackie A 16 and coxsackie A 9.[5] The first produces a striking specific eruption and this illness has been called vesicular stomatitis with exanthem.[7, 8] Pharyngeal lesions begin as small red macules, then form vesicles 1-3 mm. in diameter and then ulcerate. Similar lesions can be found on the soft palate, buccal mucosa, tongue, gingiva. The skin eruption is at first maculopapular but later some form vesicles 1.0 cm. in diameter containing a clear watery liquid from which coxsackie A16 can be cultured. The eruption is not profuse and nonpruritic.

The coxsackie A9 eruption also resembles vesicular stomatitis with exanthem with the exception that gingival and buccal mucosal lesions do not occur although the skin lesions resemble varicella except that the incubation period is brief and healing is without crust formation. Only occasionally do petechiae appear along with macular and maculopapular eruptions in coxsackie A9 infection and then it resembles Rickettseal lesions.[7]

Eruptions due to ECHO 9 infections are variegated in appearance. They have a generalized distribution and may be macular, maculopapular or even petechial. The rash appears during the fever as it does in coxsackie A16 and A9 infections. This is in contrast with the Boston exanthem in which it appears after the fever. When associated with meningitis the infection may simulate meningococcemia and this makes mandatory appropriate bacteriologic cultures to rule out this possibility. Early in the illness these patients may simulate an acute abdominal emergency and the proper decision to delay surgery at times becomes extremely difficult. To date ECHO 9 infections seem to be the most prevalent of the new exanthems and have occurred throughout the world having been recognized since 1954.[4]

These new eruptions can frequently be diagnosed at the bedside although there is sufficient overlap of the clinical pictures to make a specific etiologic diagnosis only possible by viral tissue culture. However, the illnesses are usually benign even though there were 4 cases of meningitis out of a total of 146, all of whom recovered. One fatal case of interstitial viral pneumonia was noted by Lerner's group.[4] Although our knowledge of these and other new exanthems will undoubtedly grow, the five new entities described above seem well enough studied already to be of value to physicians caring for general patients especially the pediatrician.

L.H.N.

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Corticosteroids, Antimetabolites And Other Drugs In The Treatment Of Psoriasis

About 85 different topical and systemic preparations containing tar derivatives, enzymes, hormones, vitamins and a variety of other medications are marketed for use in the treatment of psoriasis. No treatment cures psoriasis; some of these drugs are, however, useful in hastening or prolonging the remissions which characterize the natural course of the disease, though frequently the improvement is not sustained.

Recent years have seen such innovations in treatment as the use of antimetabolites and topical steroids, administered intralesionally or with occlusive dressings. The mainstay of therapy is, however, the same today as it has been for many decades—topical application of 1 to 3 per cent coal tar ointment, preferably combined with gradually increasing exposure to sunlight or other ultraviolet source.

Corticosteroids—When standard topical medications are ineffective, topical corticosteroids are worth a trial; their efficacy can be enhanced by the use of occlusive dressings. Thin flexible plastic material such as Saran Wrap (Dow) is fixed to the area of involvement after the application of a corticosteroid cream. The longer the dressings are left in place, the better the results are likely to be, but the risk of folliculitis or other infection is also increased. This risk can be minimized by frequent change of dressings. Although systemic absorption of topical corticosteroids does occur, there is no evidence that topical application, even over large areas, has produced important clinical effects such as susceptibility to systemic infections or peptic ulcer activity.

Injected corticosteroid acts more rapidly than an occlusive dressing and is particularly useful for small lesions. The main complication of this form of therapy, thinning of the skin at the injection site, occurs most frequently with the higher concentrations of corticosteroids. Systemic therapy with corticosteroids is occasionally effective but because of serious side effects associated with prolonged therapy, they should be used only as a last resort.

Antimetabolites—Although well-controlled evaluations of the folic acid antagonists aminopterin (Aminopterin Sodium—Lederle) and methotrexate (Lederle) are lacking, some dermatologists find them effective. Lederle has recently dropped aminopterin from its product line, but methotrexate is still available. Although the doses used in the treatment of psoriasis are smaller than those used in leukemia, the threat of serious toxic effects on the bone marrow remains, and frequent blood counts are mandatory. Other important toxic symptoms are stomatitis and alopecia. *Folic acid antagonists are teratogenic and should not be used in women of child-bearing age. In pregnant women, they may cause abortion.*

X-ray and other therapy—An increasing awareness of the hazards of ionizing radiation in the past decade has greatly reduced the use of x-ray therapy in the management of cutaneous diseases. Ultra superficial radiation (Grenz rays) is sometimes used to treat psoriasis refractory to topical drugs and although this type of radiation is less likely to produce chronic radiodermatitis, there are differences in opinion as to how effective it is. Although it is probable that psoriasis is a symptom of metabolic disorder, there is no reliable evidence to justify the use of oral enzymes (Lipan—Spirt; Enzypan—Norgine), or systemic or topical vitamins or dietary supplements (Nutricol—Nutrition Control Products).

The Safety Of Drugs For Intravenous Pyelography

Orabilex, an agent used for visualization of the gallbladder, was responsible for many deaths, mainly from renal failure (Medical Letter, 6:16, February 14, 1964). Its recent removal from the market has raised questions about the safety of drugs used for intravenous pyelography (IVP). Among such drugs are: Sodium Acetrizoate USP (Urokon Sodium—Mallinckrodt), Sodium Diatrizoate USP (Hypaque—Winthrop), Methylglucamine Diatrizoate USP (Renografin—Squibb), sodium diatrizoate and methylglucamine diatrizoate injection (Renovist—Squibb) and the newly released meglumine iothalamate (Conray—Mallinckrodt).

No reliable figures are available on the morbidity or mortality attributable to the use of these agents. All can cause injury or even death, mainly from hypersensitivity reactions; nevertheless, experience indicates that the risk is within acceptable limits for essential diagnostic drugs.

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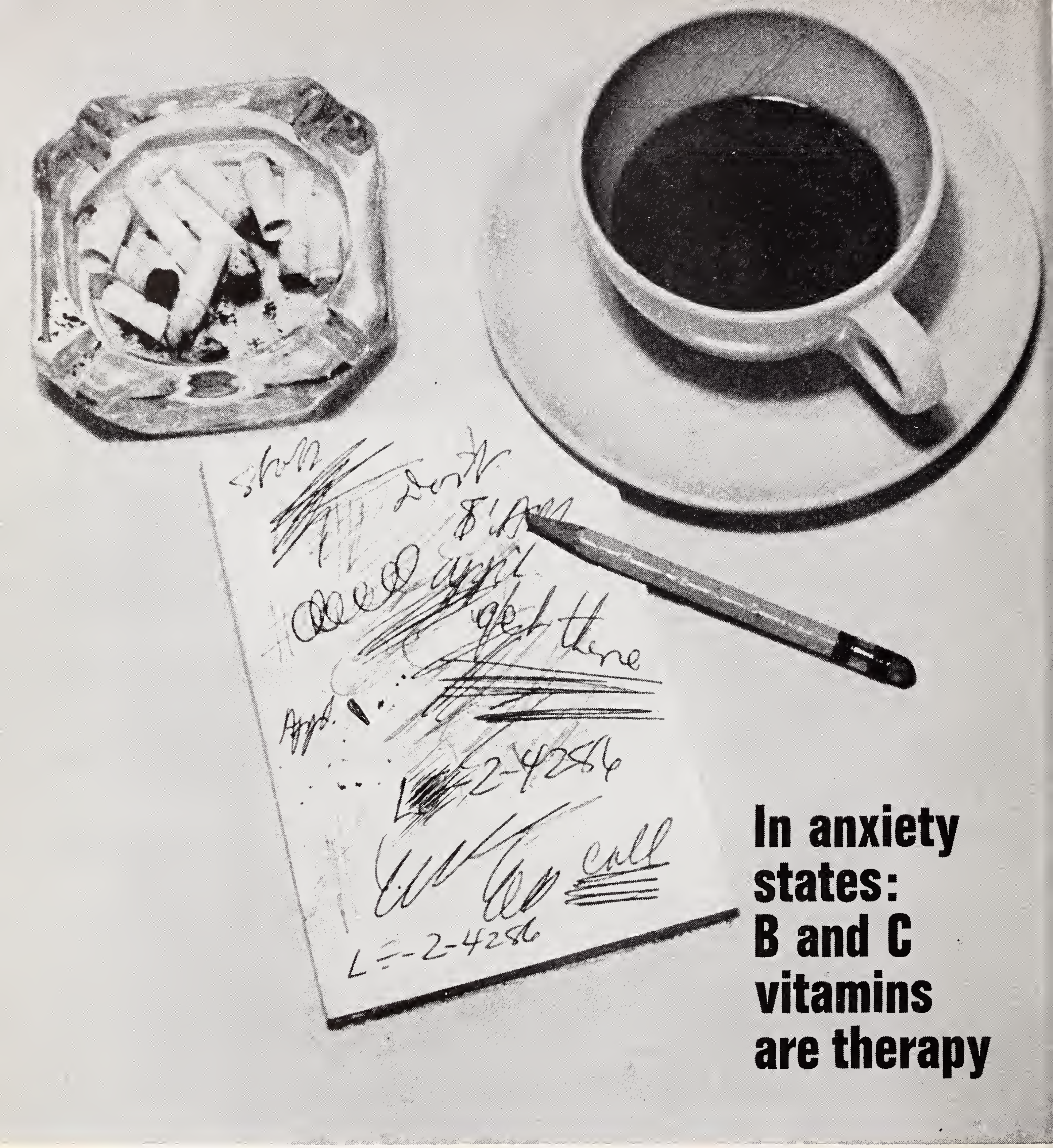

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Birth Control Problems In Connecticut

Medical Necessity, Political Cowardice And Legal Procrastination

C. Lee Buxton, M.D.

Section 53-32, General Statutes of Connecticut, Revision of 1958:

> "Use of drugs or instruments to prevent conception. Any person who uses any drug, medicinal article or instrument for the purpose of preventing conception shall be fined not less than fifty dollars or imprisoned not less than sixty days nor more than one year or both fined and imprisoned."

Section 54-196, General Statutes of Connecticut, Revision of 1958:

> "Accessories. Any person who assists, abets, counsels, causes, hires or commands another to commit any offense may be prosecuted and punished as if he were the principal offender."

In 1879, the Protestant Puritan legislature of the State of Connecticut passed the above Section 53-32. It would be laughable if it did not have such tragic consequences. Within the past 40 years, there have been 28 attempts in the State Legislature to repeal this law or change its intent (the State Legislature meets every two years), but by this time the Roman Catholic population of Connecticut had increased sufficiently to make it a political power, and every year a small but very articulate and well-organized group of Roman Catholic extremists successfully persuaded session after session to leave the law as it was. This in spite of the fact that the Catholic Church officially believes in family limitation consonant with socioeconomic necessity fully as much as Protestant or Hebrew (Pope Pius XII–Address to the National Congress of the Family Front, November 26, 1951). The difference is one of technique of restriction.

Apparently, the political implications were such (or at least such was the interpretation by members of the Connecticut legislature) that bills to repeal this law were usually not even brought out of Committee. Apparently, the courageous statesmen in our legislature are not endowed with the intestinal fortitude to face the facts of life. It was passed by a strictly Protestant legislature and considered now by educated Catholics as well as Protestants and Jews to be an unworkable tragic travesty. Parenthetically, since Connecticut has had during this time one of the lowest birth rates in the nation, one would assume that the good citizens of the State, regardless of religious persuasion, are heeding the law about as casually as the American public did the Volstead Act in the "roaring 20's."

The Connecticut State Medical Society has taken no official position on this problem.

Nobody seems to have seriously considered how this law is to be enforced. In the first place, police power, as a third party on the connubial couch, is a thought the farcical implications of which have all kinds of possibilities. Furthermore, there are few, if any, proponents of the law zealous enough to suggest the invasion of the physician's private office in the hope of interrupting a consultation at which the physician is giving his patient contraceptive advice. Also, since nothing is mentioned in this law concernng the sale of contraceptive devices, these are displayed with impunity on the drug store counter next to Chanel No. 5, fingernail polish, and hair dyes.

But there is a bitter and tragic aspect to this situation which makes it medically and economically discriminatory in a vicious way. The invasion of the private physician's office may not be taken seriously by the minions of the law, but welfare clinics providing contraceptive advice for indigent *married* women were raided and closed in 1939, physicians and nurses in attendance arrested and supplies confiscated. This has effectively prevented hospitals, welfare agencies, and other organizations from opening contraceptive clinics for the lower socioeconomic groups who cannot afford a private physician's fee. These, of course, are frequently the very people who desperately need this kind of help.

The tragic implications of this law are usually only apparent to professional personnel – doctor, social worker, visiting nurse and hospital staff. Within a few months in 1955, several of our obstetrical patients suffering from severe medical complications of pregnancy either died or suffered vascular accidents which were permanently incapacitating. These patients should never have be-

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DR. C. LEE BUXTON, Professor and Chairman, Department of Obstetrics and Gynecology, Yale University School of Medicine.

come pregnant in the first place, but they had never been able to obtain contraceptive advice. One particularly tragic case was that of a young women of 28 (G-NHCH 45-92-12) with severe mitral stenosis who had sought contraceptive advice in our clinic in vain at the time of her marriage. She died in the sixth month of pregnancy as a result of the added heart strain imposed by this condition, in spite of several months of heroic efforts on the part of the medical and nursing staff to save her. The irony of this situation in which this law was largely responsible for the death of two individuals, the mother and the unborn baby, is that following cardiac surgery she would have been able in all probability to have several children. For various medical reasons, cardiac surgery during pregnancy *in this case* (certainly not in all) was too dangerous to undertake.

Another patient with Cushing's disease partially cured by pituitary irradiation was admitted in the 22nd week of pregnancy with a blood pressure of 300+/170. Without going into too many medical details, it is sufficient to say that she had a cerebral vascular accident shortly after admission, hovered between life and death in an oxygen tent for a number of weeks during which time she was unconscious, and it was almost miraculous that she continued to live. She aborted a stillborn fetus and as a result of her cerebral accident was left with a partial right paresis and profound emotional instability. This combination of residual effects has left her completely incapacitated physically, intellectually and emotionally. One presumably minor item—the hospital costs of her stay, during which of course no professional fees were charged, amounted to $3,319, and 230 days of rehabilitation in a convalescent home cost $5,175. The couple had been unable to obtain contraceptive advice in the clinic, and, since they were not considered indigent, the hospital and convalescent home had to absorb most of the expense.

It seemed incredible from every point of view that such a state of affairs should be allowed to continue in what was generally considered to be a civilized country. A series of cases such as these was so unnecessary that the situation literally cried for correction. Since Yale University has the only medical school in Connecticut, it seemed the obvious responsibility of the Chairman of the Department of Obstetrics and Gynecology to try to do something about it. Consultation with Professor Fowler Harper of the Yale Law School resulted in a decision to challenge the constitutionality of this Connecticut law in that it violated the Fourteenth Amendment of the United States Constitution which assures all citizens of the basic civil and human rights of personal liberty. The case was heard in the lower courts of Connecticut as long ago as June of 1958, in a declaratory judgment proceeding, with the State's Attorney as the defendant. The lower court found no unconstitutionality in the state law; the decision was upheld in January of 1959 (seven months later) by the State Supreme Court and, upon appeal, was heard in the United States Supreme Court in March of 1961.

On June 19, 1961, *three years* after the original trial, the United States Supreme Court handed down its decision that it had refused to consider the constitutionality of the Connecticut law because the law was in fact a "dead issue" *and was not enforced*. This was in spite of the fact that plaintiffs' brief and argument repeatedly mentioned the impossibility of opening contraceptive clinics in Connecticut because of the law. The Supreme Court in a 5-4 decision simply evaded the issue. Since, however, the high court expressed itself in this fashion the Planned Parenthood League of Connecticut opened a contraceptive clinic on November 3, 1961—and it was closed on November 11, 1961 upon the order of the District Attorney, who stated that the clinic was acting in violation of Connecticut statutes, obviously making a considerably different diagnosis concerning the viability of this "dead issue." The leading participants in the clinic, the Medical Director and the Executive Director, were arrested and released on $250 bail apiece. Evidence concerning the activity of the clinic was obtained by members of the District Attorney's detective staff, and a trial was held on January 3, 1962 at which the culprits were found guilty, fined $100 and again released on bail when an appeal was made to the State Circuit Court of Appeals.

It was just nine months—an ironical period of gestation—before the corrected findings of the Circuit Court Judge were filed with the Appellate Court, and upon reviewing the findings the latter court concurred with the conviction and passed the case along to the State Supreme Court of Errors.

A couple of comments in the Appellate Court opinion might be of interest.

> "Much of the defendants' brief . . . is directed toward an attack on the constitutionality of this statute because of its invasion of the freedom of conjugal felicity which married couples by the natural order of society are entitled to enjoy. It is stated that an enforcement of this statute would result in an invasion of privacy, a violation of the sanctities of the home and a gross intrusion in the most sacred area of life. . . . There is no suggestion in the record that these rights have been invaded."

One can't help but wonder whether the three good and worthy judges who constitute the Appellate Court ever practiced contraception!

Another comment in the judgment is well worth quoting.

> "It is not alone for the preservation of morality in the religious sense that the legislature may have been impelled to act but also for the perpetuation of the race and to avert those perils of extinction of which states and nations have been alertly aware since the beginning of recorded history. Each civilized society has a primordial right to its continued existence and to the discouragement of practices that tend to negate its survival."

I would like to make the disrespectful suggestion that these worthy gentlemen wake up to the facts of life. There is no need here to defend the statement that the population explosion is about the most crucial problem in our world today. The case was tried in the Connecticut Supreme Court of Errors in early November, 1963, and on May 12, 1964, almost *seven months* after the hearing (which lasted about three hours), it announced its decision, upholding the lower courts. Hopefully, the clanking machinery of the law will some day relieve the State of Connecticut from the shackles of the Middle Ages. It is now 25 years since this issue was first heard in the lower courts of Connecticut and five years since the present controversy. And women in Connecticut are still unnecessarily dying because of this absurdity. The case is now being appealed to the United States Supreme Court.

Before leaving this subject, one other aspect of it must be briefly discussed. It may properly be introduced by quoting excerpts from a letter I received in December of 1960: "I am deeply interested in your test case challenging the constitutionality of the birth control law in Connecticut. You see, I have a very personal interest in birth control, because for lack of it, in one way or another, I lost a wonderful wife and mother of six children. She was only 31 years old when she died, eight hours after our last child was born.

"This was her sixth Caesarian section. Complications at birth were a rupture of the lower uterine segment, placenta previa and irreversible shock. I have gone to the County Medical Association, the doctor who delivered my six children, the priest who anointed her and the Mother Superior and Administrator of the Hospital to find out why such a tragedy happened in this day and age of medicine. I can find no justification for her death. We had asked for and received assurances that the doctor would intervene after the fourth section, but I was told that nothing could be done because my wife had run into trouble. At the time of the fifth Caesarian we felt positive that a hysterectomy would be done but I was told that since everything had gone so well that there was no need to remove the uterus. Last March that long promised and long awaited hysterectomy was performed but only as a last ditch measure. She received 23 pints of blood, 1 unit of plasma and 5 units of fibrinogen but went into irreversible shock and died.

"Regardless of whether the hospital is Catholic or not it is still a hospital and its first duty is the preservation of life. I have heard the sentiments of a few doctors on my wife's case and the usual remark was, 'Well, it was a Catholic hospital, what did the husband and wife expect would be done?' Has medicine reached the sorry state where a doctor's oath to preserve life must be outweighed by misdirected convictions of what religious ethics are involved?

"In closing I want to point out that the only method allowed Catholic parents is the rhythm system, or abstinence. Because of my wife's mentrual cycle which was thoroughly unpredictable we had to either abstain or face the wrath of the church. Abstinence in our marriage was out of the question. Contraceptives are forbidden because of our religion. What do people who find themselves in our predicament do? Men and women living together in the bonds of matrimony are also living in a life of sin because they use means to prevent further childbirth. Is the health of your wife and children to be disregarded? The Department of Welfare and all the other agencies of assistance could almost be abolished if a more realistic view were taken of this whole program. This is one of the most serious questions in the world today. It is time the Church and State sit down and discuss it openly."

It is easy to read between the lines of this letter and appreciate the anguish from which this man was and is suffering. But I do not need to be a Catholic to know that sanction could easily have been obtained for the removal of this uterus at the third or fourth Caesarian section because it was indeed a defective organ, having a thinned-out scarred lower uterine segment rendering it dangerous to this woman's health. We are well aware of the Catholic doctrine to the effect that if an operation carried out for the preservation of the life and health of a woman happens to secondarily sterilize her, the operation is therefore permissible.

Furthermore, there is a persuasive and authoritative voice in the Catholic Church which fully recognizes the socioeconomic, psychological and moral aspects in the importance of family planning. A shift in traditional attitudes is well described in a series of articles in the New York Times, August 5-8, 1963. As was mentioned previously, Pope Pius

XII stated in 1951, "We affirm the legitimacy and at the same time the limits—in truth very wide—of a regulation of offspring which, unlike so-called 'birth control,' is compatible with the law of God. One may even hope that science will succeed in providing this licit method with a sufficiently secure basis." (Address to the National Congress of the Family Front, November 26, 1951.) There is not time here to launch into a theological and moralistic discussion which, obviously, I am in no position to undertake anyway. Possibly, as Father John A. O'Brien, Research Professor of Theology at Notre Dame, said, "Catholics, Protestants and Jews are in agreement over the objectives of family planning but disagree over the method to be used." ("Let's Take Birth Control Out of Politics," LOOK Magazine, October 10, 1961.) Therefore, before becoming completely awash in a subject which I have studied extensively, may I enthusiastically recommend to Catholic and Protestant alike a book by John Rock, M.D., entitled, "The Time Has Come—A Catholic Doctor's Proposals To End The Battle Over Birth Control," published by Alfred A. Knopf in April, 1963.

In this review I have attempted to summarize the history and present status of our "Birth Control" statute and to set forth my views on why this statute should be repealed.

Fear Of The New

The mind delights in a static environment, and if there is any change to be itself the source of it. Change from without, interfering as it must with the sovereignty of the individual, seems in its very essence to be repulsive and an object of fear. A little self-examination tells us pretty easily how deeply rooted in the mind is the fear of the new, and how simple it is when fear is afoot to block the path of the new idea by unbelief and call it scepticism, and by misunderstanding and call it suspended judgement. The only way to the serene sanity which is the scientific mind—but how difficult consistently to follow—is to give to every fresh idea its one intense moment of cool but imaginative attention before venturing to mark it for rejection or suspense, as alas nine times out of ten we must do. In this traffic it is above all necessary not to be heavy-handed with ideas. It is the function of notions in science to be useful, to be interesting, to be verifiable, and to acquire value from *any one* of these qualities. Scientific notions have little to gain as science from being forced into relation with that formidable abstraction "general truth." Any such relation is only too apt to discourage the getting rid of the superseded and the absorption of the new which make up the very metabolism of the mind. —*The Collected Papers of Wilfred Trotter, F.R.S.* London, Oxford University Press, 1946, pp. 28-29.

Ventricular Fibrillation During Acute Myocardial Infarction

Sidney M. Richman, M.D., Paul A. Rudnick, M.D., David Littmann, M.D.

■ Arrhythmias occur in from 15-20% of patients with acute myocardial infarction and are generally associated with an increased mortality.[1,2] The majority of these arrhythmias are supraventricular in origin. Excluding ectopic ventricular beats, the documentation of the precise mode and time of onset of ventricular arrhythmias during acute myocardial infarction is infrequent. The diagnosis is usually presumptive in cases of "sudden death" where no obvious cause of death can be found at autopsy.[3]

The following case documents the onset of fatal ventricular fibrillation in a patient with acute myocardial infarction. It is of interest, in that the arrhythmia occurred without any preceding signs of ectopic activity and during a period not generally believed to be "vulnerable."[4]

Case Report

A 59 year old white motorman was admitted to the West Roxbury Veterans Administration Hospital for evaluation of episodic chest pain of six weeks' duration. The patient had two previously documented myocardial infarctions.

Admission physical examination revealed an obese plethoric male whose blood pressure was 180/115 mm Hg. Retinal arteriolar narrowing was noted. The second aortic sound was increased. Examination was otherwise non-contributory.

The electrocardiogram revealed an old antero-inferior myocardial infarction, unchanged from 1960. Blood chemistries, including lactic dehydrogenase and glutamic oxalacetic transaminase, were normal, but the blood sedimentation rate (Wintrobe) was 26 mm/hr.

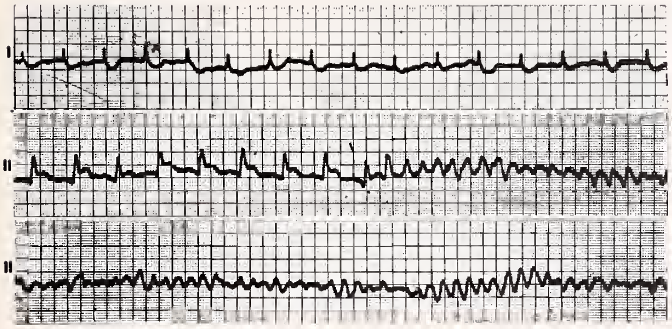

Figure I

Patient's electrocardiogram showing acute current of injury with sudden onset of ventricular fibrillation.

The patient was placed at bed rest and given supportive care. During his hospitalization, his chest pain occurred frequently. Serial EKG's showed no change. Seventeen days following admission, the patient suddenly complained of severe substernal pain. An electrocardiogram was initiated and showed an acute current of injury. However, during the course of obtaining the tracing (Fig. I) ventricular fibrillation suddenly occurred. An A.C. countershock defibrillator was applied within two minutes and terminated the fibrillation. However, attempts to restore the patient's own pacemaker were of no avail, and the patient expired. Permission for post-mortem examination was not obtained.

Discussion

It has been shown that the mortality in myocardial infarction is related to the frequency of premature ventricular beats,[5] presumably because these beats can initiate more serious ventricular arrhythmias. The most dangerous extrasystoles are felt to be those arising early in diastole, during the inscription of the T wave.[4,6] The presence of such a vulnerable phase has been documented experimentally.[7] During this critical period, a single stimulus may elicit fibrillation. However, it is noted that ventricular fibrillation in our case started well beyond the period usually considered to be hyper-irritable. This is of special importance in our present era of electro-shock therapy for control of arrhythmias, since the stimulatory shock is usually applied following the T wave, in an area not thought to be vulnerable. It may be that the presence of ischemia or infarction prolongs the period of vulnerability. This, in some ways, is similar to the propensity to atrial fibrillation seen in atrial disease. With enlarged atria, fibrillation can occur after a very few atrial ectopic beats, possibly only one, if it occurs at an appropriately brief interval following the last normal P wave.

Our case illustrates that ventricular fibrillation can start without any warning signs of irritability. The therapeutic implications of this finding remain

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unsettled. While it is generally conceded that the appearance of ectopic ventricular beats in acute infarction warrants the use of quinidine, the prophylactic value of this drug remains in doubt. Although some workers report a decreased mortality following the routine use of quinidine in acute infarction,[8] other studies show an actual increase in the incidence of sudden death in a similar group of patients on prophylactic quinidine.[3]

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I believe that by the exercise of science as well as of other intellectual pursuits mankind grows continuously into some higher form and that in some mysterious way it is in the process of transcending itself, while my own contribution to the upward trend will of course be very small, it is an immense value nevertheless, because it becomes part of a spiritual structure that is endlessly merging from amorphous matter. Science is not only an effort to gather knowledge and develop techniques for achieving mastery over nature. As Aristotle wrote two thousand years ago in his ethics, science is above all the search for understanding. Aristotle's words still convey today the very spirit of the scientific way of life. While it may never be possible to reach absolute truth, nevertheless each one of us adds a small stone to the structure of knowledge and from these efforts there emerges a certain grandeur. —Rene Dubos in the "Unseen World." Rockefeller Institute in Association with the Oxford University Press.

Rupture Of The Plantaris Tendon Misdiagnosed As Deep Calf Thrombophlebitis

Donald B. Alderman, M.D., Joseph M. Simonelli, M.D.

■ Rupture of the plantaris tendon in the calf is rarely considered in the differential diagnosis of calf thrombophlebitis. In their texts on peripheral vascular diseases, Allen Barker and Hines, Barrow, Collens and Wilensky and DeTakats make no mention of this entity. This may be a deliberate omission because it should not be difficult to eliminate this syndrome as a cause of calf pain. Clinically, however, if the history is misinterpreted a diagnosis of deep calf phlebitis may be made in patients who actually have suffered a rupture of this thin muscle or its tendon in the calf. This report is prompted by the presence of two cases of plantaris rupture at one time on the private or ward service of one of the authors, (D.B.A.) both diagnosed at some point as thrombophlebitis. Six additional similar cases have been seen in a period of four years.

Case No. 1

A 44 year old woman was admitted to the Medical Ward Service of St. Raphael's Hospital in New Haven because of a painful swollen right lower leg of less than a day's duration. Examination showed the lower leg to be warm and tender. Homan's sign was positive. A diagnosis of thrombophlebitis was made and she was treated with heparin. By the third day of heparin treatment her leg became markedly ecchymotic, and swelling and tenderness increased. Clotting time was within the usual therapeutic range. She was seen in consultation at this time and certain points in her history were obtained whose significance had previously been missed. Her calf pain had been of very sudden onset. She heard a "snap or loud click" at the time of onset, and swelling of the leg occurred within two to three hours of the initial pain. Also, the onset of pain occurred during activity (walking about the house). The diagnosis was changed to rupture of the plantaris tendon, heparin was discontinued and rest and elevation employed followed by whirlpool treatment. Pain and tenderness were much improved in twenty-four hours. All signs and symptoms were essentially negative in two weeks.

Case No. 2

A 28 year old woman felt sudden sharp pain behind her knee while breaking a stick by jumping on it. She described the pain as feeling, "As though a muscle tore." It extended down the posterior calf to the ankle. She complained of aching in the calf after the sharp pain of onset. A week later a tentative diagnosis of calf thrombophlebitis was made because of persistent mild ankle edema and marked calf tenderness and she was seen in consultation. She was admitted to Grace New Haven Memorial Hospital where examination showed the above described findings plus an area of yellow-blue discoloration of the posterior ankle region. At this point the classical history noted above was obtained from the patient and a diagnosis of rupture of the plantaris tendon made. She improved rapidly after several days of conservative management (sic infra).

In these cases the history established the diagnosis and enabled proper therapy to be employed even though a considerable time had elapsed since onset. In these and six additional cases seen by the senior author the history was remarkably similar. The patient recalled *sudden* sharp pain in the calf. In all instances the patient was ambulatory when the episode occurred and in all except one (Case #1) was engaged in some form of exertion or stretching of the legs. Stepping from a bus, jumping up and down, playing tennis or handball and bending over a file cabinet (with resultant stretching) were among the activities at the moment of onset. Three patients volunteered the information that they *heard* as well as felt a sharp snap. Illustrative of the suddenness of onset is the fact that one patient suggested that a BB shot had struck her in the calf and another thought that a stone had been thrown against his calf by a passing automobile. Five of the patients were women, three were men. Their ages ranged from 28 to 57.

Aching in the posterior calf and pain on walking was a complaint by all patients following the sudden onset. Minimal to moderate ankle swelling was present in six of eight patients. This may occur in a period of just a few hours. Calf tenderness, particularly along the medial aspect of the lateral head of the gastrocnemius muscle and/or tenderness over the Achilles' tendon, was present whether the patient was seen early or late in the evolution of the process. Ecchymosis at ankle level was seen in five of eight cases, always posterior to the malleoli. This occurred in about six hours in one patient and

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was delayed for varying periods of up to ten days in the other cases. Homan's sign was positive in six cases; in several cases in which it was employed the blood pressure cuff test was positive. This emphasizes the fact, sometimes forgotten, that these are non-specific tests and do *not* establish a diagnosis of thrombophlebitis.

The fact that all eight cases in this group were initially thought to be suffering from thrombophlebitis is due not to a high incidence of misdiagnosis of the syndrome, for indeed it is commonly seen and correctly diagnosed. Rather, it is probably due to the referral of suspected cases of thrombophlebitis to the senior author's Peripheral Vascular Disease Service. This constitutes an obvious commentary on the value of being aware of the various parameters involved in any study.

The history is all-important. If it is missed, the diagnosis of deep calf thrombophlebitis is a reasonable one in view of the calf and Achilles tendon tenderness, swelling and positive Homan's sign. While the finding of ankle ecchymosis is a physical sign which alerts one to the correct diagnosis, this evidence of deep hemorrhage may be delayed in appearance as noted above.

Treatment of this syndrome, once diagnosed, is conservative. Elevation of the leg with intermittent moist heat and the use of one of the oral anti-inflammatory enzyme preparations are prescribed. Ambulation with elastic support up to the knee and a 3/8 inch felt heel pad are employed after 48 to 72 hours. In the mildest cases, no bed rest is needed. Whirlpool and other forms of physiotherapy may be helpful. It is perhaps unnecessary to point out that the other posterior calf muscles (or their tendons) such as the gastrocnemius, soleus or popliteus can partially rupture and present a clinical picture which may be indistinguishable from plantaris rupture. Complete rupture of the larger calf muscles usually causes a palpable defect and weakness of extension of the foot.

Summary

While easily diagnosed from the history, rupture of the plantaris tendon in the calf can closely simulate the physical findings of deep calf vein thrombophlebitis. Two illustrative cases are presented and the findings in an additional six cases are discussed.

Addendum

The newest edition of "Peripheral Vascular Diseases" by Allen, Barker, and Hines, 1962, mentions the possible confusion of these two syndromes.

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Conjectures And Some Conclusions

It would perhaps be a not inept hypothesis and conjecture, not altogether deviating from the truth, which should compare a muscle fibre to a small Leyden jar, or other similar electric body, charged with two opposite kinds of electricity; but should liken the nerve to the conductor, and therefore compare the whole muscle with an assemblage of Leyden jars. Moreover that a double and opposite electricity can occupy one and the same muscle he will readily grant not contrary to the truth who has considered that a muscular fibre, although at first sight very simple, nevertheless is composed of diverse solid and liquid parts, which produce in it no slight variety of substance. —Luigi Galvani. *Commentary on the Effect of Electricity on Muscular Motion.* Translated by Robert Montraville Green, M.D. Cambridge, Massachusetts, Elizabeth Licht, Publisher, 1953, p. 61.

Pneumatosis Cystoides Intestinalis

Richard J. Cobb, M.D., Terence O'Callaghan, M.D.

■ Pneumatosis cystoides intestinalis is best described as an accumulation of gas-filled cysts of either the submucosal or subserosal areas of the gastro-intestinal tract. These pockets of gas have likewise been reported within the gastro-hepatic and falciform ligaments, the peritoneum, the mesentery and in lymph nodes. Grossly, the cysts appear as grape-like clusters usually ranging from 1 to 5 cm. in diameter, which contain only air. The prevailing concept has been that these cysts were, in fact, lymph channels distended with gas; but recently authors suggest that the cells lining the cysts are not lymphatic endothelium but rather syncytial phagocytes of repair.[1]

The condition is not uncommon in swine and has been recognized by veterinarians for many years. It was first adequately described in humans by Bang in 1876.[2] The first American reports were by Finney in 1908 and Turnure in 1913.[3,4] Since that time well over 300 cases have appeared in the literature; yet no proof of a single etiology has withstood the test of time. The four major proposed etiologic mechanisms are neoplastic, nutritional, bacterial and mechanical. Bang first put forth the neoplastic theory which postulates that the gas originates from gas forming tumor cells, but this idea has been discarded. The nutritional theory was popularized by Eveleth in 1938,[5] who was able to create these intestinal air cysts in hogs by restricting them to a polished rice diet. He also noted that if corn was added to this polished rice diet the condition did not occur. There is no correlation between dietary habits and the intestinal emphysema in the human cases found in the literature. The bacterial theory is based on the assumption that gas-forming organisms invade the bowel wall, producing intestinal emphysema. The mechanical theory stems from the fact that many cases previously reported are concomitant with conditions causing mechanical obstruction and with inflammatory diseases of the gastro-intestinal tract, or follow trauma secondary to sigmoidoscopy or surgery.

Recently gastric emphysema has been described associated with chronic pulmonary disease by Plachta and Speer.[6] They suggested the gastric emphysema arose as a complication of pulmonary bullous emphysema. Keyting et al[7] proposed alveolar rupture, pneumomediastinum, and retroperitoneal air advancing along peri-vascular routes to the wall of the bowel. A mechanical etiology would seem likely in these cases.

Recently a patient seen at The Hospital of St. Raphael with pneumatosis coli showed on rectal biopsy a microscopic tract connecting the lumen of the bowel with one of the submucosal cysts. We present this case as the first known reported case in which a connection between these cysts and the large bowel mucosa was demonstrated histologically.

Case Report

R. Z., a 57 year-old, white female was admitted to the hospital on March 25th, 1963.

For 6 to 8 weeks prior to admission she gave a history of intermittent diarrhea, accompanied by crampy abdominal pain. The stools were never bulky in amount, nor more than 5 to 6 per day, and were said to be watery and occasionally blood-streaked. She treated herself with proprietary medication without relief. She visited her physician on March 23rd, who felt and observed on proctoscopic examination multiple spongy, glistening and elevated lesions in the rectum. Previous to this examination, she had not been examined rectally or vaginally for two years.

She was a known diabetic and hypertensive, and was being treated with oral medications for both conditions. The only previous surgery was a Caesarian Section twenty-four years previously. She stated that no appendectomy was done at that time. She had been mildly constipated for several years. Her past and family histories were otherwise noncontributory.

Physical examination revealed an obese, nervous, white female who did not appear acutely ill. Her blood pressure was 168/80 and all other vital signs were normal. Her chest and abdomen were negative. On rectal examination multiple, spongy, crepitant, bleblike areas were palpated giving a similar sensation as one gets when palpating subcutaneous emphysema. They involved practically the entire circumference of the rectum. The upper limits could neither be felt nor visualized in sigmoidoscopy. Some of the lesions bled rather easily during the latter examination. Other findings were negative.

X-Ray examination of the chest revealed slight left ventricular enlargement. The lung fields were clear. No evidence of emphysema or pulmonary fibrosis was seen. Plain film of the abdomen showed clusters of discrete, lucent areas on the entire left side of the abdomen following the course of

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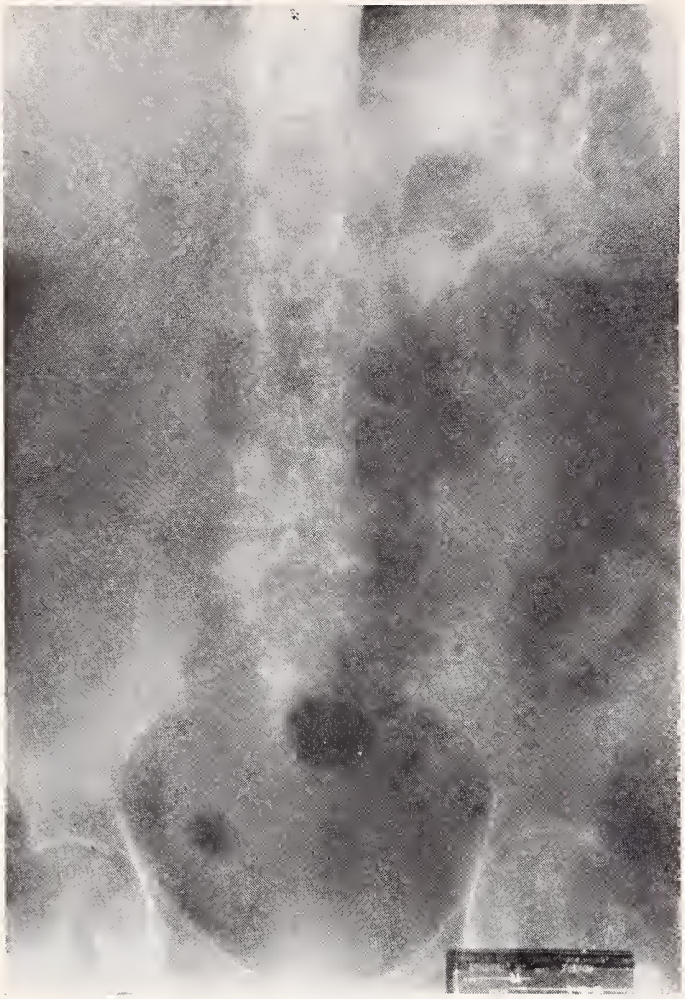

Figure I

Plain film of the abdomen showing pneumatosis cystoides coli.

the distal one-half of the colon. (Fig. I) A barium enema showed the discrete lucent areas to be adjacent to the intestinal lumen from the splenic flexure to the rectum. These clusters of lucent areas produced filling defects which are pathognomonic of pneumatosis coli. A G. I. Series demonstrated a small direct hiatus hernia. An oral cholecystogram showed good function, and a single lucent stone was noted within the gallbladder.

The hemogram and electrolytes were within normal limits. The blood sugar was 165 mgm% and the urea nitrogen was 14 mgm%.

On March 28th, sigmoidoscopy with biopsies at 12 cm. was done. On microscopic examination these biopsy pieces consisted of large bowel mucosa and submucosa. Two of these biopsies showed pathological changes consisting of cystic spaces in the submucosa which contained giant cells, precipitated protein and erythrocytes. These cysts showed a lining partly composed of swollen endothelial-like cells (Fig. 2) and the cysts were surrounded by hyperplastic fibrous tissue which was moderately infiltrated by histiocytes and eosinophils. The giant cells had a prominently eosinophilic cytoplasm which in some cells was vacuolated; their nuclei, which varied from one to twenty-four in number, were small, dark, oval-shaped, and were arranged predominantly peripherally within the cells. One biopsy specimen showed a tract which in some areas was lined by cells resembling endothelium, connecting a submucosal cyst with the mucosal surface. (Fig. III) This tract contained foreign material (feces) scattered throughout the entire length; similar material was present within the cyst. The characteristic eosinophilic giant cells were also present within this tract at both mucosal and submucosal levels. Although the giant cells appeared to surround the foreign material, none could be seen within the giant cell's cytoplasm. Following symptomatic treatment only, the patient was discharged greatly improved on the 12th hospital day.

Following discharge, there has been a progressive reabsorption of the submucosal air as seen on repeated plain films of the abdomen. Three months after the onset of the present illness, the number and size of these cysts has decreased by approximately three-quarters. The patient has had no symptoms referable to her gastrointestinal tract since discharge.

Summary And Conclusion

This is a case of pneumatosis cystoides intestinalis in which the clinical and radiological diagnosis was confirmed histologically following rectal biopsy. A mucosal defect connected by a tract to a submucosal cyst was demonstrated microscopically. Both the cyst and tract showed the characteristic microscopic

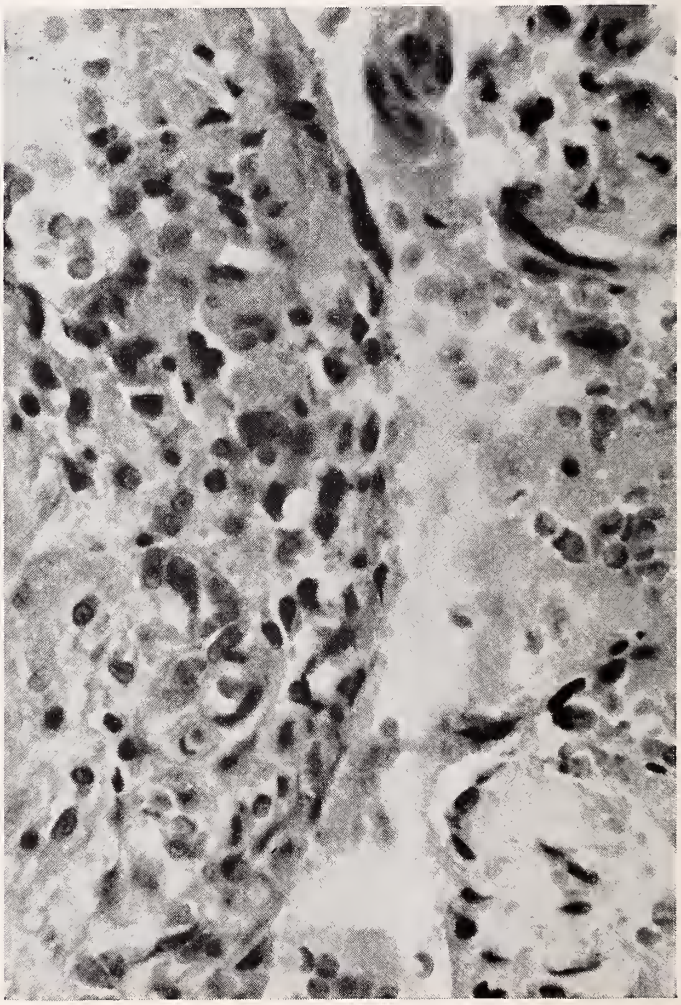

Figure II

High-power view of cells lining the cyst and tract.

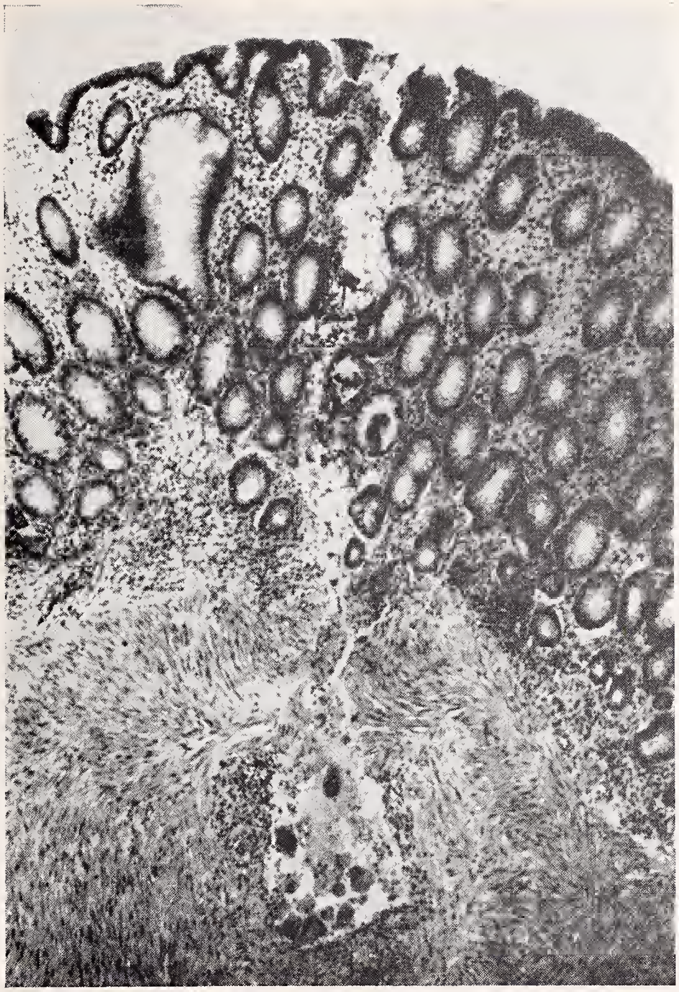

Figure III

Rectal biopsy showing submucosal pneumatoid cyst and tract leading to the mucosal surface.

findings of pneumatosis coli, and fecal material was found within both the cyst and the tract. In this case either the mechanical or bacterial theories previously mentioned could be postulated. A mucosal defect caused by pressure due to increased gas formation in association with the patient's diarrhea would allow intraluminal gas into the bowel wall. Gas-forming bacteria from the lumen could also have gained entrance through this defect and caused cyst formation. The gas, when in the submucosa, caused a prominent foreign body type granulomatous reaction. With this portal of entry, subsequent submucosal spread could have caused further cyst formation along the bowel, as we have seen in this case.

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The physician needs a clear head and a kind heart. —Sir William Osler. *Aphorisms From His Bedside Teachings and Writings.* Edited by William Bennett Bean, M.D. New York, Henry Schuman, Inc., 1950, p. 80.

Experiences With Seventy-Five Consecutive Retinal Detachments

Marvin L. Sears, M.D.

Introduction

■ The purpose of this report is to present a brief account of experience obtained with 75 consecutive cases of retinal detachment during the period September 1961 to September 1963. Development of this study has been made possible by the cooperation of several ophthalmologists throughout the state of Connecticut. This series has several advantages which facilitate its evaluation: 1. it consists almost exclusively of fresh detachments, 2. geographical considerations lend themselves to a close follow up of patients, 3. all cases have been operated upon by the author with uniform technique, i.e. exclusively with the use of indirect ophthalmoscopy, scleral grooving, and silicone material as described by several writers, most prominently by Schepens *et al.*[1]

Methods

All patients received complete general physical and ophthalmologic examinations, including detailed fundus drawing of both retinas, following indirect ophthalmoscopy and scleral depression. The overwhelming majority of patients were operated upon within one week after initial examinations, and usually, although not always, within two to three weeks after initial symptoms. Except in the case of large or giant horseshoe tears, no special efforts were made to enforce preoperative bed rest. Seventy-two operations were performed under local anesthesia with 2% xylocaine and adrenalin. Three were done under general anesthesia. Following canthotomy, peritomy, and placement of stay sutures around the four recti muscles (efforts were made to avoid disinsertion of muscles), localization of retinal breaks was done with indirect ophthalmoscopy while surface diathermy was applied to the sclera using the Walker diathermy machine. A scleral groove was then made at the appropriate site. Its length and width were dictated by the size and number of the retinal breaks. Waxed white silk mattress sutures size 4-0 were then placed. A silicone belt was passed through the groove, and tacked circumferentially to the sclera in at least two quadrants. If a silicone implant was to be used, it was then slipped under the strap. Supplemental diathermy was frequently used in the groove. Drainage of subretinal fluid was performed as described by Pierce.[2] Closure of the scleral groove and tightening of the silicone belt was then accomplished with tonometric control. A tantalum clip was ordinarily used for permanent tying of the silicone belt. If a muscle was disinserted, it was reinserted with gelfilm under it. The peritomy and canthotomy were then closed.

Post-operatively, the patients were treated with systemic tetracycline for five days, topical steroids and dilatation, and were ambulated generally within five days.

Results

Table I indicates the predominant type of retinal break found in this series of detachments. In this small group, predominance of equatorial tears as compared with tears at the ora serrata was noted. In the aphakic group, the distribution was more nearly equal. Of some interest in this latter group of patients was the relatively frequent history of *recent* cataract surgery, performed within two or three months prior to the development of retinal symptoms. In thirty-one of the 75 patients only a single tear could be found. In this group with single tears, 12 patients had large single horseshoe breaks (1.5 mm. or greater).

Figure I is a scattergram comparing preoperative with postoperative visual acuity and serves as a

TABLE I
PREDOMINANT TYPE OF RETINAL DETACHMENT

Break	*Phakia*	*Aphakia*
Ora serrata	8	9
Equator	42	6
Dialysis	6	1
Schisis with detachment	3	—
	59	16

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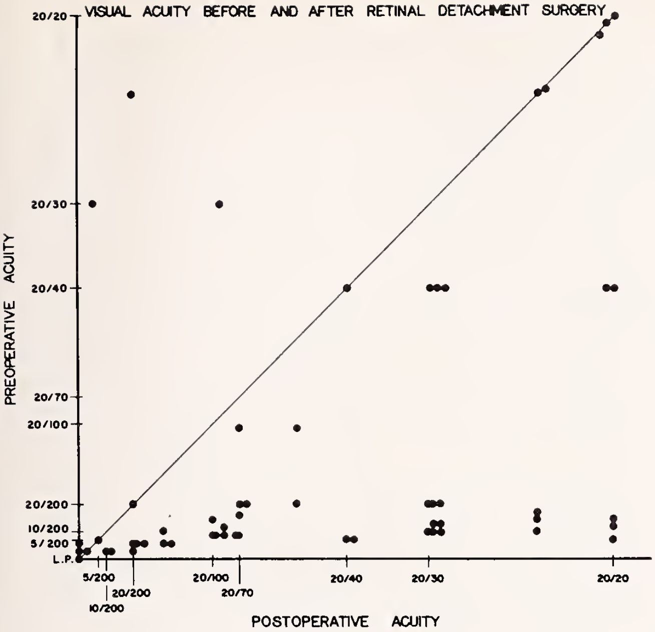

FIGURE I

partial basis for evaluating the results of retinal surgery performed. Only patients who were postoperative more than six months are included. As can be seen, the majority of patients in this series had the macula included in their retinal detachment, but the effect of early surgery was to restore the visual acuity. The final values for acuity cannot be evaluated until more time elapses, but the trend is toward progressive improvement.

Table II lists surgical failures. These are defined in two categories: 1. Those patients whose retinas remained unattached. Six of 75 patients fell into this category. 2. Those patients who had a successful reattachment operation, but whose visual acuity had nevertheless decreased. Two of 75 patients fell into this group. Three of the six patients who had unattached retinas were aphakic patients whose vitreous was considerably inflamed and degenerated in appearance preoperatively. One of the two remaining patients had a severely traumatised eye that fell questionably within an operable category. Case #5 had a successful reattachment of the retina for six months. Then, a new break developed, associated with moderately severe vitreous reaction and fixed folds in the retina. A second operation did not reattach the posterior pole. A third attempt with liquid silicone injection also failed. The remaining patient demonstrated persistent vitreous traction on the flap of the tear in spite of a second operation. Further surgery was declined. Of the four patients whose retinas were attached but in whom the visual acuity decreased, one had a severe vitreous reaction, possibly the result of excessive diathermy. A second developed a fixed macular fold.

TABLE II
FAILURES AFTER RETINAL DETACHMENT SURGERY

A. *Retina unattached*	*Type*	*Cause*
1. #A9-57-93	aphakia, single horseshoe	excessively high buckle, bridged and torn by progressive vitreous bands
2. #59-02-50	traumatic, 180° dialysis	massive vitreous bands
3. #59-27-50	phakia	persistent traction on flap of horseshoe tear
4. #59-14-56	aphakia	massive vitreous retraction
5. #59-47-02	phakia, multiple equatorial	massive vitreous retraction
6. #79-63-40	aphakia	massive vitreous retraction
B. *Attached retina, poor visual result*		
1. #57-85-29	aphakic, single horseshoe	fixed macula fold
2. #56-07-64	multiple equatorial	severe vitreitis

Table III shows complications that occurred either during surgery or in the postoperative period. Of considerable interest is the absence of postoperative infection, either within the orbit or within the globe. A second feature worthy of comment is the absence of any systemic complication in this group of patients.

Table IV lists causes for reoperation. A large percentage of patients in this group had continuing vitreous traction requiring further intervention, either an additional buckling procedure and/or vitreous injection. It was possible in two of three patients with new breaks seen six months or more after primary retinal surgery to effect a reattachment of the retina.

Comment

The scattergram of visual acuity (Figure I) facilitates interpretation of visual results. Five patients had a worsened visual acuity (see Table II). Eight patients had unchanged visual acuity. Forty-seven patients showed an improvement in visual acuity.

Among complications, infection was absent. Three patients, however, did develop granulomas. In each case the granuloma had developed where

TABLE III
COMPLICATIONS OF RETINAL DETACHMENT SURGERY

Type	*Cause*
1. Choroidal hemorrhage (2)	drainage
2. Globe perforation (2)	stay suture placement
3. Granulomatous episcleritis (3)	silk sutures uniting strap
4. Subscleral silicone implant (2)	deep scleral groove
5. Limited ductions (2)	necrosis, fibrosis of muscle
6. Massive intraretinal exudation (1)	?

TABLE IV

Reasons for reoperations	Approach
1. Elevated intraocular pressure (1)	Strap loosened
2. Buckle too far posteriar (3)	Flap dissected anteriorly
3. Subscleral silicone implant (2)	Repositioning of implant
4. Previously undetected break (1)	Diathermy and buckle
5. Continued vitreous retraction (5)	(see text)
6. New breaks in untreated retina (3)	Diathermy and buckle

silk sutures and not a tantalum clip had been used to tie the ends of the encircling silicone strap. One patient in the series developed massive intraretinal exudation following his retinal detachment operation. This reaction greatly resembled circinate retinopathy and suggested some circulatory embarassment to the retina as a result of his buckling operation. In recent months, however, there has been complete clearing of the exudation. In two patients a deep scleral groove was associated with suprachoroidal presentation of the silicone implant in the vitreous cavity in the early postoperative period. In both patients suturing of the sclera at the base of the old groove and replacement of an overlying silicone implant in the sclera adjacent to the original scleral groove proved successful.

The most difficult problem to solve was the presence and/or development of vitreous retraction (Tables II and III). In two instances saline injection into the vitreous cavity through the pars plana following a routine buckling procedure was unsuccessful. In two patients liquid silicone injection (Dow Corning), done after an unsuccessful buckling procedure, resulted in reposition of the retina onto the previously diathermized buckle with subsequent reattachment of the retina. In several patients, however, (Table II) severe vitreous retraction accounted for failure of retinal reattachment.

Two choroidal hemorrhages occurred during drainage in this series. In both instances there was a slow progressive absorption of the choroidal hematoma with no deleterious effect upon the final outcome. The performance of drainage under magnified visualization of the choroid as recommended by Pierce[2] has greatly reduced the incidence of choroidal hemorrhage.

The reattachment rate resulting in this series was 92% (69 of 75) and compares favorably with other recent reports.[1] These results with silicone buckling may be compared with those recorded for simple diathermy by Smith and Pierce[3] in 1953 where a 70% success rate was found. Certainly results obtained with present day methods contrast sharply with those reported prior to the use of indirect ophthalmoscopy and scleral buckling.[4]

Now that accurate localization and sealing of retinal breaks can be performed, it would appear that the chief obstacle to the favorable outcome of retinal detachment surgery lies with the reaction that sometimes is present or develops within the vitreous cavity.

Conclusions

A preliminary report on the therapy of seventy-five consecutive retinal detachments is presented. The results and complications are discussed. It is hoped that with continued observation further experience may be gained from a long term follow up of these patients.

Acknowledgment

The author is grateful to the ophthalmologists who helped make this study possible and wishes to thank the resident staff at the Yale-New Haven Medical Center who contributed to the medical and surgical care of these patients, and also Miss J. Wilnechenko and Miss M. Zuklampen in the Dana operating room for their expert operative assistance.

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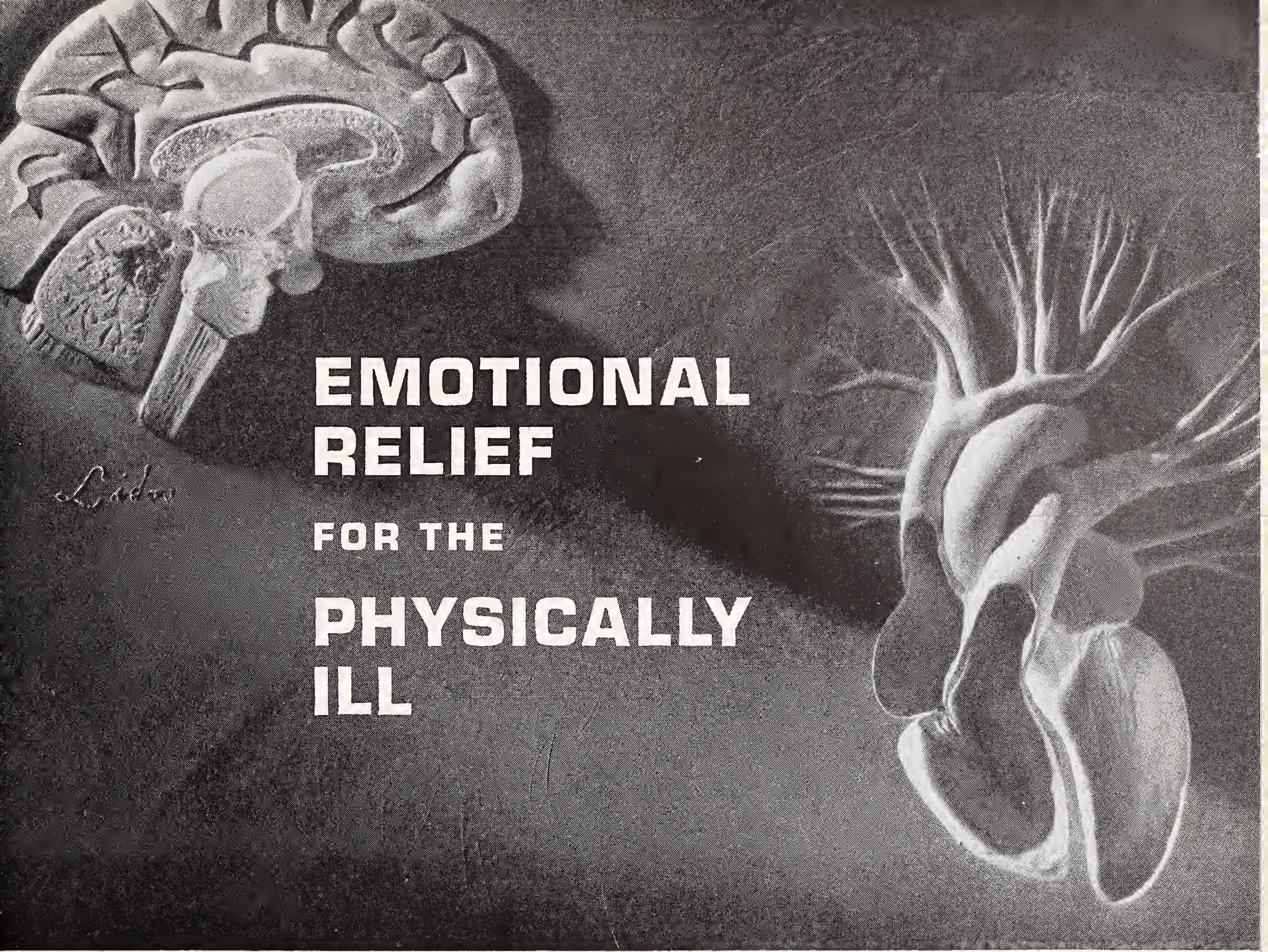

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Precautions: Should administration of meprobamate cause drowsiness or visual disturbances, the dose should be reduced. Operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Prescribe cautiously and in small quantities to patients with suicidal tendencies. Massive overdosage may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after prolonged use at high dosage.

Complete product information available in the product package, and to physicians upon request.

Usual adult dosage: One 400 mg. capsule or two 200 mg. capsules at breakfast; repeat with evening meal.

Supplied: 'Meprospan'-400 (meprobamate 400 mg.), 'Meprospan'-200 (meprobamate 200 mg.), each in sustained-release capsules. Both potencies in bottles of 30.

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THE PRESIDENT'S PAGE

Early in June a very comprehensive report entitled PHYSICIAN-HOSPITAL RELATIONS was distributed by the AMA to all the delegates, alternate delegates and State Society presidents. It represented the culmination of three years of intensive study by the Committee on Medical Facilities of the Council on Medical Service. That it is up to date is indicated by the fact that developments in both professional and legal aspects occurring in 1963 are included.

Space does not permit more than a summary of its outline. After tracing the policies adopted and modified by the House of Delegates from 1930 to the present, it discusses the implementation of these policies and finds that there is a significantly large segment of the hospitals and medical staffs that do not follow these policies or are unaware of them. It then goes on to discuss its findings from many studies and surveys on Graduate Education, Medical Finance, Expansion of Hospital Functions, and Regulation of Medical Care.

It is not only a very informative report, it is, or should be, an even more disturbing report so far as the medical profession is concerned. Throughout all its conclusions and recommendations there may be discerned two parallel lines of thought. The first is the continual and ever increasing pressure of lay agencies—hospital governing boards, labor unions, and government both state and national—to assume greater control over, and regulation of, not only medico-economic factors but even the qualifications for staff membership and the practice of medicine itself. Among other facts it cites instances of legislative acts and judicial decisions establishing qualifications for staff appointment and acceptance of individuals deemed by a medical staff as not qualified.

The parallel train of thought is that the medical profession itself has contributed to a significant degree in the development of the trend to more and more assumption of hospitals in providing medical services that should properly be done in physicians' offices. Likewise we contribute significantly to the pressure for public controls by our failure to carry out fully our own self-government. All accredited hospitals have a medical staff organization and committee structure that provides the mechanism to accomplish this. While the great majority of medical staffs do a creditable job of self-discipline, there have been, and are, too many instances where failure to carry it out have been seized upon to invoke measures of lay and public control. To quote from the report: "Such voluntary controls have proved adequate when effectively applied. However, survey findings and third party comments stress that voluntary controls are not being uniformly applied and that, in fact, many medical staffs are not functioning properly. . . . Voluntary controls need continuing vigorous application if the principle of self-government is to be retained."

This report should be in the hands of every president or chief of the staff of every hospital. It should be carefully studied. The officers, chiefs of departments, and staff committees should evaluate their own organizational structure and more importantly how effectively it functions. Medicine must demonstrate even more than heretofore its willingness and ability to police itself, or it will lose at an ever increasing rate its freedom for self-government.

Ralph L. Gilman, m.d.

THIRTY-NINTH CONNECTICUT CLINICAL CONGRESS

OF THE CONNECTICUT STATE MEDICAL SOCIETY AND THE YALE UNIVERSITY SCHOOL OF MEDICINE

Yale-New Haven Medical Center — Mary S. Harkness Memorial Auditorium
333 Cedar Street, New Haven, Connecticut

Friday, September 25, 1964

9:00 Registration (Coffee will be served in the lobby until 9:30)

Morning Session

9:45 Welcome and Opening Remarks—
Ralph L. Gilman, *Storrs, President, Connecticut State Medical Society*

CORRECTABLE RENAL VASCULAR DISEASE

Marvin Lillian, *New Haven, Presiding*

10:00 Diagnosis of Correctable Renal Vascular Disease
John P. Merrill, *Boston, Mass.*

10:30 Treatment of Correctable Renal Vascular Disease
Michael E. DeBakey, *Houston, Texas*

11:00 Panel Discussion:
Moderator: William Dock, *Brooklyn, N. Y.*
Panelists: John P. Merrill, Michael E. DeBakey
Radiologist: Gilbert S. Melnick, *New Haven, Conn.*
Urologist: Bernard Lytton, *New Haven, Conn.*

11:45 Intermission

John C. Leonard, *Hartford, Presiding*

12:00 Clinical Pathological Conference
David M. Spain, *Brooklyn, N. Y.*
Discussant: William Dock
Radiologist: Gilbert S. Melnick

1:00 Luncheon

Afternoon Session

CORRECTABLE CEREBRAL VASCULAR DISEASE

Gilbert H. Glaser, *New Haven, Presiding*

2:30 Natural History of Atherosclerotic Cerebral Vascular Disease
H. Houston Merritt, *New York City*

2:50 Diagnosis of Correctable Cerebral Vascular Disease
John Stirling Meyer, *Detroit, Michigan*

3:10 Medical Treatment of Correctable Cerebral Vascular Disease
Joseph F. Fazekas, *Washington, D. C.*

3:30 Surgical Treatment of Correctable Cerebral Vascular Disease
Charles G. Rob, *Rochester, N. Y.*

3:50 Panel Discussion
Moderator: H. Houston Merritt
Panelists: John S. Meyer, Joseph F. Fazekas, Charles G. Rob
Radiologist: James H. Scatliff, *New Haven, Conn.*

COME FOR THE WEEKEND—Attend the Clinical Congress on Friday, and the following activities on Saturday, September 26th, Surgical and Medical Grand Rounds at the Yale-New Haven Medical Center on Saturday morning and the University of Connecticut-Yale Football game on Saturday afternoon. Tickets may be obtained from the Yale Athletic Association, Yale Station, New Haven.

Luncheon for visiting physicians will be served in the cafeteria of the Grace-New Haven Community Hospital.

The registration fee of $5.00 provides for admission to all sessions of the Congress. Hospital residents and interns and medical students will be admitted without charge, if a statement of their position, signed by an official of the hospital or school, is presented at the registration desk.

PLAN NOW TO ATTEND

THE DERMATOSES THAT WERE STEROID-UNTREATABLE

Salt and water retention, edema, overstimulation of the appetite, excessive weight gain, mood swings—these were some of the problems that used to confront physicians when they wanted to prescribe steroids for dermatoses. For patients already overweight, or with edema associated with cardiovascular disease, or those who were tense and anxious, steroid treatment could aggravate their problems. But with the advent of ARISTOCORT® Triamcinolone, many of these patients became "steroid-treatable." The reason: Not only did *this* steroid provide gratifying symptomatic relief, but it did so *without* the penalty of overstimulation of the appetite, excessive weight gain, salt and water retention, edema, and undesirable euphoria. And these benefits have been confirmed for other patients with steroid-susceptible disorders, as well as those formerly untreatable.

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A single daily dose may provide effective control, is convenient for the patient, and can be employed in both initial and maintenance therapy.

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CAPSULE REPORT ON ACTIONS OF THE HOUSE OF DELEGATES AMERICAN MEDICAL ASSOCIATION — 113th ANNUAL CONVENTION

June 21-25, 1964 — San Francisco

(*See the July 6 issue of AMA NEWS for further details on the major House actions.*)

Tobacco and health, human rights, physician-hospital relations, continuing medical education, the cost of medical care, and federal subsidization of prepayment plans and health insurance companies were among the major subjects acted upon by the House of Delegates at the American Medical Association's 113th annual convention held June 21-25 in San Francisco.

Dr. Donovan F. Ward of Dubuque, Iowa, vice-president of the Association, was named President-Elect of the Association. He will become President at the June, 1965, annual convention in New York City, succeeding Dr. Norman A. Welch of Boston, who was installed at the inaugural ceremony in San Francisco.

The AMA 1964 Distinguished Service Award was won by Dr. Irvine H. Page, director of research of the Cleveland Clinic, for his investigation of cardiac, vascular and renal disease.

Final registration figures reached a grand total of 49,437, including 14,229 physicians.

Tobacco and Health

The House approved a strong stand on tobacco and health by calling cigarette smoking "a serious health hazard." This action was taken after the reference committee on Public Health and Occupational Health considered 10 resolutions and a Board of Trustees report on the subject and heard considerable testimony.

In adopting a four-point reference committee report, the House said "the American Medical Association is on record and does recognize a significant relationship between cigarette smoking and the incidence of lung cancer and certain other diseases."

It urged that programs be developed to disseminate vital health education material on the hazards of smoking to all age groups through all means of communication. The House also recognized the contribution of the Surgeon General's Committee in its comprehensive report. And it emphasized that a joint committee of the AMA and the National Education Association already has adopted a resolution urging elementary and secondary schools to include programs on smoking and health in their health education curricula.

The House further recommended that the AMA pamphlet, "Smoking: Facts You Should Know," should be modified "in the light of accumulating knowledge."

Finally, the House said that the delegates and the Board of Trustees "should take great pride in the establishment of the research program on tobacco and health that is being carried out by the AMA Education and Research Foundation."

In adopting the report of the AMA-ERF the House called attention to the following statement:

"The Board of Directors of AMA-ERF and the Board of Trustees of the AMA were clearly aware of the possibility of criticism in accepting this grant (10 million dollars from several tobacco companies). But against that possibility they weighed the potential benefits to the public who will continue to smoke and concluded that the risk was insignificant by comparison. The only hope of minimizing the hazards of smoking lies in research which points to the course that the AMA as well as others must take."

Human Rights

On the major issue of human rights the House declared itself "unalterably opposed to the denial of membership, privileges and responsibilities in county medical societies and state medical associations to any duly licensed physician because of race, color, religion, ethnic affiliation, or national origin."

This action was taken after the reference committee had heard a detailed discussion and had considered four resolutions on the subject.

In addition, the House called "upon all state medical associations, all component societies, and all individual members of the AMA to exert every effort to end every instance in which such equal rights, privileges and responsibilities are denied."

The House also accepted a report from the Board on the liaison committees of the AMA and the National Medical Association. This report reviewed the history of the committees and noted that "great progress has been made voluntarily. More progress can reasonably be expected in the immediate future, especially if the committees are permitted to continue on a constructive, cooperative basis. This requires effort, but more importantly, good will and the desire to eliminate problems."

Physician-Hospital Relations

Conclusions and recommendations in a significant and extensive report on physician-hospital relations were adopted by the House. Prepared by the Council on Medical Service's Committee on Medical Facilities, the report stresses "the imperative need for the medical profession to assume responsibility for the quality, continuity, and availability of professional services and for the coordination of these services with the other essential supportive aspects of health care."

The report's recommendations are designed to serve as guidelines for physicians in meeting the problems involved in the changing patterns of care such as: appointment of salaried chiefs of staff; appointment of salaried heads of clinical departments; appointment of salaried directors of medical education; employment of salaried physicians for outpatient and emergency departments; use of salaried physicians to provide care ordinarily provided by interns and residents; and utilization of closed-panel prepayment medical care programs by hospitals.

The report also includes a review of the development of AMA's policy on physician-hospital relations, a study of the relation of policy to actual practice, and an investigation of the factors influencing change—including graduate education, medical finance, expansion of hospital functions and regulation of medical care.

Continuing Medical Education

Authorization was made by the House to establish an AMA-sponsored survey and accreditation program in continuing medical education. In the program attention will be concentrated on institutions and organizations offering courses rather than on individual courses, and appraisal of an institution's or organization's program will be carried out only at its request.

Eventually, approved institutions or organizations will be so designated in the Council's annual lists of "Continuing Education Courses for Physicians," and when all institutions which wish to list their courses have had the opportunity to be considered for approval, only courses of approved institutions and organizations will be included in the annual list. Programs will be surveyed by a Review Committee on Continuing Medical Education.

Cost of Medical Care

A four-volume report of the AMA Commission on the Cost of Medical Care was received by the delegates, and the House concurred with the Board of Trustees that the conclusions and recommendations of the Commission will be studied and a report will be made to the House for its consideration at the 1964 Clinical Convention.

The four volumes include a General Report on factors involved in medical care costs, a full report on "Professional Review Mechanisms," another on "Significant Medical Advances," and one on "Changing Patterns of Hospital Care."

In its report the Board said that the Commission "is aware that its efforts will not result in a magic reduction in the price of medical and hospital services. It does believe, however, that its study has produced a considerable amount of new and relevant information which will serve as a basis for better understanding by the public and the medical profession of this complex subject."

Reaffirmed the AMA policy favoring federal grants for "bricks and mortar" — funds for construction and renovation of medical schools, hospitals, related institutions, and mental health centers—but urged that the "advantages and desirability of multiple source financing be kept clearly in mind." The House also was informed by the Board that it is appointing a commission to conduct a broad study of the role of federal support of medical research.

Other Actions

The House went on record as opposing federal subsidization of prepayment plans and health insurance companies, and it asked for an AMA study of the development of state programs which utilize prepayment plans or health insurance companies in the implementation of state programs of medical aid to the aging under the Kerr-Mills law.

A proposal to poll all AMA members concerning compulsory Social Security for self-employed physicians was rejected by the House. In addition, the House concurred with the reference committee in opposing polls of the membership on issues of "great or even moderate importance" because the House members express the majority sentiments of their constituents on all questions coming before the House.

An expanded program on medical ethics was endorsed by the House. The program will be designed to educate physicians and the public on what medical ethics means to them and how medical ethics affects them. The Judicial Council, working with the Board of Trustees, will determine the means by which this expanded program is to be implemented.

Approval was given to a change in the Bylaws to allow the House to set the hour and day of election of AMA officers at the Annual Convention. This was adopted early in the House session and made it possible to have the nominations on Wednesday afternoon and the elections on Thursday morning.

A three-point communications program designed to improve the public relations position of the medical profession was endorsed by the House on recommendation of the AMA Committee on Communications. The program includes a redoubling of efforts by county and state societies, closer liaison with media personnel and prompt information to state societies on AMA news releases and testimony.

Miscellaneous Actions

In considering a wide variety of resolutions and reports, the House also:

Approved the creation of the Section on Allergy on recommendation of the Board of Trustees.

Approved a comprehensive inquiry of the causative factors for the sharp increase in syphilis and gonorrhea and urged the AMA to "take leadership in educational and research measures designed to control and eliminate syphilis."

Okayed a national conference on area wide planning of hospitals and related health facilities, to be sponsored under the auspices of the AMA.

Agreed to continue and broaden studies on the problems of unwed mothers, illegitimacy and other related matters and to develop positive preventive programs.

Supported a position statement on protecting children against physical abuse and called for legislative guidelines to the states relative to legislation on this matter.

Asked the Board of Trustees to investigate establishment of a wire communications system between AMA headquarters in Chicago and offices of state medical associations.

Referred to the Council on Medical Service a resolution condemning the practice by some hospitals of adopting constitutions which deny staff privileges to physicians not eligible or certified by specialty bodies or societies.

Agreed with the Board that a forum for representatives of national medical specialty societies and the American Academy of General Practice be held on November 1, 1964, in Chicago.

Approved a resolution calling for the publication of the proposed nominees for standing committees (councils) of the House be submitted in advance of the Annual Convention, preferably in the House of Delegates Handbook.

Recommended that the Board of Trustees use the talents of Dr. Edward R. Annis, immediate past president, and other qualified spokesmen for medicine with appropriate remuneration.

Asked the Committee on Insurance and Prepayment Plans of the Council on Medical Services to consider a revision of simplified health insurance claims forms.

Recommended that the Board of Trustees approve the establishment of an ad hoc study on family practice as proposed by the Council on Medical Education.

Agreed with the change of name of the Council on Medical Education and Hospitals to the Council on Medical Education.

Requested clarification of the ethical and legal limitations of physicians participating in court-ordered, pre-trial psychiatric examinations.

Urged the AMA to continue its vigorous opposition to tax regulations discriminating against "professional associations" and "professional corporations," and its support of legislation which seeks to provide tax equality with business corporations for "professional associations" and "professional corporations."

Opening Session

Dr. Edward R. Annis of Miami, outgoing AMA president, told the special Sunday afternoon opening session that a greater effort is needed in the areas of continuing medical education and health education programs. He also urged state and county medical associations to bolster their paid executive personnel to help carry out local, state and national projects. Doctor Annis called for an increase in AMA dues and later the House referred the question of a dues increase to the Board of Trustees for study and for a report at 1964 Clinical Meeting in Miami. Honored at the opening session were the presidents of state and territorial medical associations and a number of special AMA guests from national organizations.

At the Monday session awards announced were the AMA Scientific Achievement Award to Prof. Rene Jules Dubos, Ph.D., of the Rockefeller Institute, New York City, and the Joseph Goldberger Award in Clinical Nutrition to Dr. William J. Darby of Vanderbilt University School of Medicine, Nashville.

Inaugural Ceremony

Doctor Welch, in his inaugural address Tuesday night, said that medicine must be united if it is "to serve the public in the future to the high degree that it has in the past." He stressed that American physicians must be "standing strong and firm with a heart and a conscience tuned to public need, with a respect for the rights and privileges of the individual, and with an abiding faith in our free competitive system of medical practices."

In keeping with Doctor Welch's address, "Unity in Medicine," presidents or their representatives from 29 medical specialty organizations were honored guests at the ceremony.

The Distinguished Service Award was presented to Doctor Page and the Scientific Achievement Award was given to Doctor Darby.

Wednesday Session

Speaking at the Wednesday session, Doctor Welch pointed up the growing alliance between medicine and research—an alliance rooted in truth, knowledge and the freedom to search them out. He called these "the greatest assets available for human development and human well-being." Doctor Welch also enumerated the important projects of the AMA in the past year such as mental health, continuing medical education, tobacco and health, and AMA-ERF, the Institute of Biomedical Research.

Election of Officers

In addition to Doctor Ward, the new president-elect, the following officers were named:

Dr. Carlton Wertz of Buffalo, vice-president; Dr. Milford O. Rouse of Dallas, speaker of the House, and Dr. Walter C. Bornemeier of Chicago, vice-speaker.

Dr. Robert C. Long of Louisville was re-elected to the Board of Trustees for a three-year term, and Dr. Alvin J. Ingram of Memphis was elected to a three-year term. Doctor Ingram replaces Dr. R. B. Robins of Camden, Ark.

Nominated and elected to the Judicial Council was Dr. Charles C. Smeltzer of Knoxville, Tenn.

Named to the Council on Medical Education were Dr. William P. Longmire of Los Angeles, and Dr. William A. Sodeman of Philadelphia.

Elected to the Council on Medical Service was Dr. John Rumsey of San Diego, and re-elected was Dr. Willard A. Wright of Williston, N.D.

Dr. William A. Hyland of Grand Rapids, Mich., was re-elected to the Council on Constitution and Bylaws.

TIME OUT . . . *to mark this special day on your calendar*

SEPTEMBER 25, 1964

39th CONNECTICUT CLINICAL CONGRESS

of the

Connecticut State Medical Society

and the

YALE UNIVERSITY SCHOOL OF MEDICINE

to be held in

MARY S. HARKNESS MEMORIAL AUDITORIUM — YALE-NEW HAVEN MEDICAL CENTER

333 Cedar Street, New Haven, Connecticut

It will be a one-day program beginning at 9:30 A.M. and adjourning at 5:00 P.M.

FRIDAY, SEPTEMBER 25, 1964

— WATCH YOUR MAIL AND THE JOURNAL FOR COMPLETE INFORMATION —

a symbol of CONNECTICUT'S VOLUNTARY PLAN
TO HELP PAY DOCTORS' BILLS . . .

IT'S PART OF CONNECTICUT
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221 WHITNEY AVENUE, NEW HAVEN, CONNECTICUT

Committee On Maternal Mortality And Morbidity

Hemorrhage

Prenatal Course

■ This 25-year-old primigravida was first seen by her physician at the end of the first trimester. At that time the red count was 3.6 M. and the hemoglobin was 64 per cent. She was given "routine calcium, iron, and vitamins" and subsequently was seen regularly by her doctor. Weight gain was 20½ pounds. X-ray pelvimetry revealed the pelvis to be adequate. The past history was negative.

Labor

For about twelve hours prior to admission the patient had been having mild uterine cramps and slightly bloody "show." She entered the hospital at 12:45 A.M. At that time her membranes were intact, her blood pressure was 118/88, her contractions were irregular.

First Hospital Day

7:00 A.M. The patient was given meperidine HCl.[1] 100 mg.; scopolamine HBr. 0.3 mg.; pentobarbital Na.[2] 0.2 gm.

8:00 A.M. Sterile vaginal examination: cervix 2 cm. dilated and well thinned out; membranes were ruptured artificially. During the day repeated rectal examinations were done. Uterine contractions were ineffectual, and there was very little descent of the head.

7:00 P.M. Meperidine HCl. 100 mg.; scopolamine HBr. 0.3 mg.; pentobarbital Na. 0.2 gm. (approximately 19 hours after admission).

8:00 P.M. Oxytocin[3] 0.2 cc. intramuscularly, were given to stimulate contractions.

9:00 P.M. On rectal examination the cervix was found to be approximately 5 cm. dilated.

9:30 P.M. 1,000 cc. glucose and water intravenously; fetal heart good; descent slow. (First recorded attempt to hydrate patient.)

10:15 P.M. Meperidine HCl. 75 mg.; scopolamine HBr. 0.4 mg. Patient was very restless with her contractions and complained of a great deal of back pain.

11:00 P.M. Oxytocin 0.25 cc. intramuscularly, was given; fetal heart good; contractions had increased to a frequency of 2 to 3 minutes, lasting 40 seconds.

Second Hospital Day

1:00 A.M. Meperidine HCl. 100 mg.; scopolamine HBr. 0.2 mg. (This was approximately 24 hours after admission.)

2:45 A.M. Meperidine HCl. 100 mg.; fetal heart good.

5:30 A.M. Meperidine HCl. 100 mg.; scopolamine HBr. 0.2 mg.

6:30 A.M. Cervix fully dilated.

Delivery

Under gas, oxygen and ether anesthesia the patient was delivered by midforceps (Scanzoni rotation, ROP to OA). Delivery time was 7:02 A.M. A living infant weighing 8 pounds, 1 ounce was born. After the delivery, Oxytocin 1 cc. was given intramuscularly. Examination of the birth canal revealed the presence of a bilateral laceration of the cervix. The placenta was then expressed (presumably intact—no details were given). The cervix and the episiotomy were then repaired. At this point an infusion of 1,000 cc. of 5 per cent glucose was begun. The uterus was reported to be contracting well. Approximately one hour after delivery it was noted that the fundus was quite soft. Oxytocin 0.5 cc. was then put into the infusion! (No mention is made of blood pressure in the first hour after delivery.) Because of the persistent bleeding with passage of clots and continuing atony of the uterus, oxytocin 1 cc. and ergotrate 0.2 mg. were given intravenously. The patient was quite restless. Morphine sulfate 10 mg. was given intramuscularly. A transfusion of whole blood was started, and during this procedure the patient became extremely restless. Her blood pressure continued to drop, her pulse was weak and thready, and she began to have air hunger. Oxygen was started, and a second transfusion was begun in the other arm. In view of the low blood pressure, 500 cc. of Expandex was started. The blood pressure remained imperceptible. Uterine atony persisted. Afibrinogenemia was ruled out on the basis of the considerable amount of clotted blood noted. It was felt that secondary hemorrhage associated with uterine atony was present. A total abdominal hysterectomy was therefore started at about 9:00 A.M. At operation no intra-abdominal bleeding was found. The entire uterus was intact. After the operation the patient's condition slowly improved. At 10:30 A.M., approximately three and one-half hours postpartum, the blood pressure could be obtained for the first time since the vascular collapse. Three hours later the blood pressure was 92/0, pulse 140, respirations 32, and oral temperature 101°. The blood pressure continued to rise, the patient received more blood transfusions and her condition further improved. There was moderate vaginal bleeding. The indwelling catheter drained bloody urine, and the output was practically nil. It was the pathologist's opinion that a temporary kidney shut-down had occurred. This he attributed to shock and rapid infusion of blood. At 11:00 P.M. (approximately 14 hours after surgery) the patient was digitalized and transfused because of marked fluctuation in pulse and blood pressure. Two hours later the blood pressure was 78/56, oral temperature was 104°, and a moderate amount of bright red vaginal drainage continued. Most of the blood was clotted. At this time the patient had a chill, and it was felt that this was probably caused by a transfusion reaction. Diphenhydramine[4] HCl. 20 mg. was given intramuscularly. The blood pressure remained low throughout the day, and the patient complained of back pain and thirst and was given several ounces of fluid orally. Approximately 30 hours after hysterectomy the patient complained of some shortness of breath. Because of considerable abdominal distention, a Levine tube was passed. Within a few seconds after the tube was in place, she suddenly became cyanotic and gasped for air, and the pulse became almost imperceptible. More digitalis was given. Oxygen was administered. Both the blood pressure and the pulse began to rise, the latter reaching 130. A pelvic examination was performed, and a "tremendous' amount of clotted blood was removed from the vagina. Inspection of the vagina revealed the area to be completely intact. A vaginal pack was inserted. The patient's condition went progressively downhill, and she expired at 10:00 P.M., approximately forty-eight hours after admission and thirty-six hours after hysterectomy.

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[1] Demerol—Winthrop Laboratories.

[2] Nembutal—Abbott Laboratories.

[3] Pitocin—Parke-Davis & Co.

Autopsy Diagnoses

Postpartum hemorrhage, massive; intraperitoneal and retroperitoneal hemorrhage, postoperative. Kidneys showed changes characteristic of lower-nephron nephrosis.

Comments

1. Routine iron was prescribed for rather severe anemia. No record reports subsequent blood counts during the pregnancy. Anemia left the patient ill-prepared for hemorrhage.

2. The patient was obviously in prodromal rather than real labor when admitted to the hospital. Adequate evaluation at this time and sedation for the night would have been of value.

3. Massive doses of sedatives throughout labor, begun before labor was established, prevented good physiological labor in this primigravida and enhanced inertia. Administration of sedatives in a primigravida not in actual labor with cervical dilatation less than 4 cm. usually does lead to inertia and paves the way for trouble. One hour after the first large group of analgesics and sedatives was given the cervix was only 2 cm. dilated. The amount of such drugs that this patient received between admission time and reaching second stage is incredible.

4. Oxytocin was given repeatedly for stimulation of a labor which had been sabotaged and made inert by unwise medication.

5. Oxytocin was given in what would generally be considered as rather dangerous doses. The intravenous route, with a slow, regulated drip, is safer than the intramuscular one, but if the latter is used, surely 0.05 cc. is a dose ample for stimulation. To give .25 cc. intramuscularly is to invite tragedy.

6. Obstetrical consultation should have been obtained.

7. Operative delivery of this primigravida was performed when the cervix had been fully dilated for only one-half hour. Furthermore, she had an occiput posterior position. What was the reason for the hurry? Was there any fetal distress? There is no mention of such. Why, then, could not the obstetrician have waited for further descent of the head and possible anterior rotation to occur, rather than to have rushed in prematurely to perform an elective forceps rotation?

8. In view of the inert labor, postpartum inertia with consequent hemorrhage should have been anticipated. In other words, crossmatching of blood should have been performed earlier. Adequate parenteral fluids should have been administered in labor to combat dehydration.

9. Exploration of the birth canal, including the uterus, is mandatory after midforceps operations.

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[4] Bendryl HCl.—Parke-Davis & Co.

10. The hysterectomy was probably unnecessary, was obviously ill-timed, and was a desperate gesture which gave the *coup de grace*. The massive intraperitoneal and retroperitoneal hemorrhage resulted from the performance of the hysterectomy in the presence of vascular collapse. The uterus was found to be intact but atonic. Surely, the repeated large doses of meperidine and the ether anesthesia could well have made it so. During the critical hour after delivery, no record of blood pressure and pulse was made. Had the patient survived the acute episode, one wonders about the ultimate survival possibilities because of the renal shut-down. Lower-nephron nephrosis and bilateral renal cortical necrosis are well known sequelae to massive obstetrical hemorrhage and shock. Or was the scanty bloody ooze from the catheter the result of an operative injury to the bladder at the time of the hysterectomy? Probably not, as the autopsy report does not mention laceration of the bladder.

11. Why was a vaginal pack inserted when the vagina was intact and unlacerated? It could serve no purpose except to conceal temporarily bleeding from higher areas in the birth canal!

12. In summary, was not the whole case the result of ignoring the old obstetrical adage of leaving things to nature in the absence of obvious complications, and of smoking a long, black cigar?

The Medical Profession: Human Understanding and Peace

Because of the nature of our profession, born to care for the health of men, of all men, protecting them against misfortune, we cannot remain coldly indifferent, like mere spectators, to the visible menace of our age.

Each day the world sickens more with distrust and fear, bringing us at times to the verge of despair. It falls to us to play our part to uproot these evils, to serve the cause of human understanding, to fight to ensure peace; that peace which is the slogan of no man because it is the banner of all men whatever their country, their colour, or their religion may be; that peace sought by him who follows Buddha, by him who believes in the God of Mahomet, and by him who prays to Christ; that peace to which all men of goodwill on the earth aspire. —*Dr. Ignacio Chavez.* Speech delivered at the Inaugural Ceremony of the IV World Congress of Cardiology. Universidad Nacional Autonoma De Mexico, Mexico D.F., 1962, p. 10.

AROUND THE STATE

News From Yale University School Of Medicine

Dr. Max Theiler, the Nobel Prize-winning Director of the Rockefeller Foundation Virus Laboratories, and Dr. Wilbur G. Downs, an Associate Director for Medical and Natural Sciences of the Rockefeller Foundation, have been appointed to the faculty of the Yale University School of Medicine as full professors.

The appointments, announced by Charles H. Taylor, Jr., Provost of Yale, are effective immediately.

The two distinguished doctors are coming to Yale in connection with the transfer of the Rockefeller Foundation Virus Laboratories from New York City to New Haven. The Rockefeller Laboratories will occupy three floors of a new nine-story building now under construction at Yale and expected to be completed later this year.

Both Dr. Theiler and Dr. Downs will retain their present positions with the Rockefeller Foundation Virus Laboratories which will continue to operate as a separate and independent unit after its transfer to Yale. But the Rockefeller scientists will hold appointments to the Yale medical faculty.

Dr. Theiler, who won the Nobel Prize in physiology and medicine in 1951 for his development of a yellow fever vaccine, has been appointed Professor of Epidemiology and Microbiology.

Dr. Downs, who is in charge of the Rockefeller Foundation's world-wide virus research program, has been appointed Professor of Epidemiology.

Yale's new $4,200,000 Laboratory of Epidemiology and Public Health will be the new headquarters for the Rockefeller Foundation Virus Laboratories. The Department of Epidemiology and Public Health at the Yale Medical School will occupy the other six floors of the nine-story building.

The Rockefeller Foundation is supporting the building project with a $1,500,000 grant.

Since 1950, the research work of the Virus Laboratories has been concentrated on arthropod-borne viruses that affect both man and animals, and both Dr. Theiler and Dr. Downs are authorities in this field. Arthropods from a large division of the animal world that includes all insects, spiders and ticks.

The Virus Laboratories, from its home base in New York City, services field laboratories in California, Trinidad, Brazil, Colombia, and India, and collaborates with dozens of other laboratories around the world.

Dr. Theiler has been a staff member of the Rockefeller Foundation since 1930, and director of the Virus Laboratories since 1951. He developed his famous 17D vaccine for yellow fever in 1937.

Before joining the Foundation, he served as an Assistant and Instructor in Tropical Medicine at Harvard University from 1922-30.

Dr. Theiler was awarded the Chalmers Medal of the Royal Society of Tropical Medicine and Hygiene in 1939, the Flattery Medal by Harvard University in 1945, and the Lasker Award by the Lasker Foundation in 1949.

Dr. Downs has been at Yale since February, 1962, as Visiting Professor of Epidemiology, and has been assisting in arrangements for the move of the Virus Laboratories.

In 1952, he was named director of the Foundation's Regional Virus Laboratory in Trinidad, and served in that post until 1961, when he was appointed an associate director of the Foundation.

Four physicians on the faculty of the Yale School of Medicine have been promoted to the rank of full Professor effective immediately, it was announced recently by Provost Charles H. Taylor, Jr.

Promoted are Dr. Clarence D. Davis, to Professor of Obstetrics and Gynecology; Dr. Daniel X. Freedman, to Professor of Psychiatry; Dr. Richard H. Greenspan, to Professor of Radiology, and Dr. Elias E. Manuelidis, to Professor of Pathology.

Dr. Davis was appointed to the Yale faculty in 1957 as an Associate Professor. He came to Yale from the University of Missouri Medical School, where he had been Professor and Chairman of the Department of Obstetrics and Gynecology.

He is a graduate of the Massachusetts Institute of Technology and the medical school of Johns Hopkins University, and has also served on the medical faculties of Duke University and the University of Washington.

In addition to his Yale duties, he also serves as an attending obstetrician and gynecologist at Grace-New Haven Community Hospital.

Dr. Freedman, who received a B.A. degree from Harvard University in 1947, earned his M.D. degree at Yale in 1951. He was appointed to the faculty in 1955 as Instructor in Psychiatry, promoted to Assistant Professor in 1958, and to Associate Professor in 1961.

A specialist in the field af psychopharmacology, he was named a career investigator in mental health by the National Institutes of Health in 1957. He also is a consultant to the Veterans Administration Hospital in West Haven.

Dr. Greenspan was named to the faculty in 1960 as Assistant Professor of Radiology, and promoted to Associate Professor in 1961. Previously, he had served on the faculty at the University of Minnesota.

He was graduated from Columbia University with a B.A. degree in 1945, and from Syracuse University with an M.D. degree in 1948. He also serves as an attending radiologist at Grace-New Haven Community Hospital, and as a consultant to the Veterans Administration Hospital.

Dr. Manuelidis, who earned his M.D. degree at the University of Munich in 1942, came to Yale in 1951 as a Research Assistant in Preventive Medicine and Pathology. He was named an Instructor in 1952, Assistant Professor of Pathology in 1955, and Associate Professor in 1958.

Previously, he had been director of the Pathological-Anatomical Laboratory and later, an assistant in the Neuropathology Laboratory at the German Research Institute for Psychiatry.

At Yale, he also is Curator of the Brain Tumor Registry, and an attending pathologist at Grace-New Haven Community Hospital.

Board Of Governors New Haven County Medical Association

June 25, 1964

A regular meeting of the Board of Governors of the New Haven County Medical Association was held at the Colonial House, Hamden, on June 25, 1964 with Dr. Jack Galen presiding.

The usual large attendance of the Board was augmented by the presence of honorary guest members: Doctors Jachin B. Davis, Clyde Deming, John Freiheit, A. J. Mendillo and Samuel B. Rentsch.

The Board spent considerable time discussing the report of Dr. J. H. Green, Chairman of the Committee on Medical Ethics and Deportment. His committee has reviewed another case involving the theory of "Master and Servant," in this case a surgeon and an anesthetist. They held the former should be blameless, but under the present Connecticut law this does not conform.

What has compounded the seriousness of this matter is the illness of the surgeon which has taken him out of practice and his assets completely tied up by the plaintiff's attorney. It was pointed out that neither county or state societies have ever made provisions helping a fellow practitioner in such an emergency. The Board took certain steps to relieve the doctor for the present. Resolutions will be considered at future meetings of our Board to avoid the placing of members in such jeopardy.

The meeting was followed by dinner at which our guest, Mr. Joseph Duplinsky, President of Connecticut Blue Cross, exchanged ideas about increased cost of hospital care with mutual benefit to Mr. Duplinsky and the members of the Board.

Respectfully submitted,

H. A. Levin, M.D., *Clerk*

New London County

The Scientific Session of the New London County Medical Association was held on June 4, 1964 with the president, Casimer Bielecki, M.D., presiding. Arrangements were made by Duncan MacDougall, M.D., of Groton for a tour of the facilities of the Electric Boat/General Dynamics Corporation. Following this tour, the Association were guests at a dinner meeting at Holiday Inn, Groton. The medical director of Prudential Iife Insurance was the speaker of the evening.

Nursing Liaison Activities In State Medical Societies

An important objective of the Committee on Nursing is to work closely with state medical societies and particularly with those committees responsible for maintaining liaison with members of state nursing organizations. Prior to developing a definitive program geared to the needs of the states, the Committee believed it was essential to ascertain the extent of nursing liaison activities in all of the state societies. To elicit information for this program, the staff prepared a questionnaire which was forwarded to 52 state societies early in 1963. The following is a sampling of the information gleaned from the data:

—Forty-one of the 50 state societies responding conduct active liaison programs of one type or another with nursing groups. In 27 of these societies, meetings are called by either nurses or physicians. A committee on nursing, or comparable group, is responsible for liaison with nursing organizations in 35 states.

—Of the subjects most frequently discussed at joint meetings, nursing education, the physician-nurse relationship, patient care, and the shortage of nurses represent concerns of the physician.

—Suggestions for improving the nurse-physician relationship, in order of their highest frequency of occurrence, were to improve understanding and communication through joint effort (eg, jointly planned refresher courses), to establish nurse liaison within the states, and to meet frequently with nursing groups.

—Significant to the work of the Committee were suggestions for ways in which the AMA Committee can best serve the state societies in strengthening the nurse-physician relationship. Most frequently mentioned were assisting in establishing nurse liaison within the states and providing information on other state programs, informing state societies on problems and trends in nursing education and service, and holding nurse-physician meetings at the national level.

The findings of the survey would indicate that in terms of future programming the committee will concern itself with the following objectives:

1. To devise a means of communicating with state societies in order to keep them informed on nursing problems and trends.
2. To prepare a simple guide to assist those state societies having no liaison activities with nursing groups to develop formal programs and to expand and strengthen present programs of existing committees.
3. To consider national and regional follow-up conferences after the first national conference for physicians and nurses.

In conclusion, a questionnaire for the purpose of eliciting information on liaison programs and activities with nursing groups was forwarded to 52 state societies. Fifty (96 per cent) of the societies responded. Forty-one of the 50 respondents (82 per cent) presently maintain liaison with the nursing profession in their state. It is important to note that nine states, including several with a high percentage of nurse and physician population, evidently have no forum for the exchange of ideas or for joint effort.

In order to develop a program to assist the state medical societies in initiating and/or implementing their nurse liaison activities, the Committee on Nursing conducted a survey to assess the current status of nurse liaison in each state society. The members of the AMA Committee on Nursing believe the findings of this study are of particular interest to physicians, and have therefore authorized the publication of this report.

Florence M. Alexander, RN, PhD, *Secretary*

Members of the Committee on Nursing are Arthur A. Kirchner, M.D., *Chairman,* Clarence H. Benage, M.D., Elias S. Faison, M.D., Benson W. Harer, M.D., Charles L. Leedham, M.D., and Edmund D. Pellegrino, M.D.

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SMJAB INCORPORATED

Alfred J. Jackson is retired as President and Treasurer of the State Medical Journal Advertising Bureau, Inc., on July 1, but will continue his service to the State Journal Group in a consultant capacity.

Coming to the American Medical Association on July 23, 1907, Mr. Jackson spent his entire business life in the field of scientific medicine. When the Bureau—then known as the Cooperative Medical Advertising Bureau—was reorganized in December, 1945, Mr. Jackson was appointed Director by the Board of Trustees. In December, 1955, the Bureau was formally separated from the A.M.A. and Mr. Jackson was elected President of the new corporation.

The following tribute, prepared by Dr. Stanley B. Weld, former Chairman of the Advisory Committee, expresses the esteem and affection with which Mr. Jackson is regarded. This tribute appeared in the Newsletter of the State Medical Journal Advertising Bureau.

A Tribure To Alfred J. Jackson

"To Alfred J. Jackson upon his approaching retirement we pay our tribute to a man of sterling character, an efficient business executive who has carried on his duties with competence and unfailing good judgment.

Coming to the Bureau on the recommendation of the Board of Trustees of the American Medical Association almost twenty years ago, he was unknown to the editors and business managers of the various State Medical Journals comprising the Bureau. In a short period of time Mr. Jackson won the confidence and respect of those with whom he came in contact and the Bureau flourished under his guiding hand.

It is with deep regret that the Board of Directors of the Bureau loses Mr. Jackson as its President and herewith records its unanimous appreciation of his devotion to it.

May the coming years of retirement bring to him the rewards of friendships cultivated far and wide and may he long continue to enjoy good health and a happiness so well deserved.

For the Board of Directors of the State Medical Journal Advertising Bureau,

Stanley B. Weld, M.D.

Attest: Frank B. Ramsey, M.D.,
Chairman, Board of Directors,
State Medical Journal Advertising Bureau, Inc."

Doctor's Office

Arnold M. Baskin, M.D., announces the association of Peter Demir, M.D., for the practice of urology at Madison Towers, 111 Park Street, New Haven.

Louis W. Daley, M.D., announces the relocation of his office for the practice of otorhinolaryngology from 32 Gove Hill, New Britain, to Old Boston Post Road, Old Lyme.

Donald S. Dworken, M.D., announces the opening of an office for the practice of orthopedic surgery at 881 Lafayette Street, Bridgeport.

William H. Gallaher, M.D., announces the opening of an office for the practice of internal medicine at 380 Boston Post Road, Orange.

William A. Gryboski, M.D., announces the opening of an office for the practice of general vascular and chest surgery at Cedar Lake Medical Center, 73 Cedar Street, New Britain.

Ferenc Husvet, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 66 Maple Avenue, Collinsville.

Lewis M. Karas, M.D., announces his association with Jerry Goldfarb, M.D., for the practice of internal medicine and gastroenterology at 19 Third Street, Stamford.

William Knights, M.D., announces the opening of an office for the practice of pediatrics at 11 Central Avenue, East Hartford.

James Labraico, M.D., announces the opening of an office for the practice of allergy at 300 Main Street, Bristol.

Stewart J. Petrie, M.D. and Melvin B. Laubstein, M.D., annouce the relocation of an office for the practice of obstetrics and gynecology from 153 Main Street, Ansonia, to 56 Minerva Street, Derby.

David P. Reed, M.D., announces the opening of an office for the practice of cardiology and internal medicine at 47 Holmes Avenue, Waterbury.

Edward M. Segall, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 152 Meadow Street, Naugatuck.

Nathaniel Selleck, M.D., has returned to Danbury to become associated with Dr. Paul Kunkel at 30 Hospital Avenue. In his association with Dr. Kunkel, he will specialize in internal medicine and cardiology.

Joseph B. Shaw, M.D., announces the opening of an office for the practice of psychiatry at 320 Main Street, Manchester.

Richard A. Stamm, M.D., announces the opening of an office for the practice of psychiatry at 85 East Avenue, Norwalk.

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OBITUARIES

M. Heminway Merriman, M.D.

1877 - 1964

Dr. M. Heminway Merriman who specialized in ear, nose and throat, was born August 1, 1877 in Watertown, in the house where he lived most of his adulthood. He was the son of the late Henry and Mary Ann (Heminway) Merriman.

He attended Waterbury High School, graduated from Taft School in 1897, and from Yale University in 1901. He received his medical education at Columbia College of Physicians and Surgeons in New York City graduating in 1906, serving his internship and residency at Saint Luke's Hospital in New York City. He then joined the staff of Saint Luke's Hospital where he practiced general medicine for several years before specializing in otolaryngology in 1918. Dr. Merriman then became a member of the special staff at Saint Luke's, the Clinical Staff at Bellevue Hospital, and a consulting otolaryngoligist at Staten Island Hospital. In 1924 he was appointed a member of the otolaryngology staff of the Waterbury Hospital, and began practicing otolaryngology in Waterbury, becoming a member of the honorary staff approximately twenty-four years later, but never fully retiring until the last few years of his life.

In 1924 he converted his mother's summer home in Watertown, which was now his, into a year-round home, after deciding to bring up no more of his children in New York City. The family home on the corner of Prospect and Grove Streets in Waterbury was converted into an office building with an apartment on the upper floor. He was associated there originally with Dr. Carl Munger.

Dr. Merriman had many other interests outside his profession. In 1926 he decided to become a "gentleman farmer" and purchased land on the Northfield Road, Watertown comprising nearly four hundred acres. In addition to farming he kept about thirty-five cows, work horses, and riding horses. He and the late Leonard Carley were instrumental in founding the Watertown Riding Club, and later he was instrumental in starting the first Watertown Hunt of which he became Co-Master of Fox Hounds with the late Dr. Andrew J. Jackson. On his 80th birthday he had a horseback ride with two other octogenarian friends.

Dr. Merriman was always interested in and active in sports. In 1904 he traversed the length of the Rhine River in Germany with a companion in a folding canoe, which had never been done before, and because of this was made a member of the Explorer's Club of New York.

In the 1920's he became a member of the Tunxis Hunting and Fishing Club in Tolland, Mass. and bought a cottage there in 1927 which still remains in the family.

During the depression years he provided employment for needy individuals by buying land adjacent to his own on Northfield Road, and having it cleared to make a beautiful little pond which he stocked with bass. It is now listed on U. S. Geological Survey Maps as Merriman's Pond.

In addition to riding, hunting, and fishing, Dr. Merriman was an avid golfer and a member of the Connecticut Senior's Golf Association, and one time president of the Watertown Golf Club.

A few years ago Dr. Merriman was the recipient of the Citation of Merit, the highest accolade of the Taft School Alumni Association. He was a former trustee of the Taft School.

He was past president of the Waterbury and New Haven County Medical Societies, a member of the New York Academy of Medicine, Waterbury and the Connecticut State Medical Societies. A Fellow of the American College of Surgeons and a diplomate of the American Board of Otolaryngology. He was a member of Alpha Deta Phi Fraternity and of the Eliau Honor Society. He also belonged to the Sanctum Club of Litchfield, the Waterbury Club, and the University Club of Litchfield County.

He was also a past president of the Sons of the American Revolution, and a member of the Society of Colonial Wars of the State of Connecticut.

Dr. Merriman's three sons were in military service during World War II and he conceived the idea of putting out a weekly mimeographed news letter for them and other relatives and friends who were in the service, which he called the Merriman Chronicle. Excerpts from letters he received from his readers and news from home composed the Chronicle which went to about twenty different people in service all over the world. At the end of the War the Merriman Chronicle ceased to function and Dr. Merriman and his faithful secretary, Mrs. Bertha Smith, put all the issues together and made bound volumes for each of his children and one each for the Yale Library and the State Library in Hartford.

Dr. Merriman will be remembered for his kindness, his gentleness, his gentlemanliness—and his absent mindedness. Stories about the latter are numerous and there was always a standing offer at the Waterbury Hospital of a reward for anyone who could find his medical bag.

Dr. Merriman is survived by his wife, Mrs. Sally Mallory (Betts) Merriman, three sons, Dr. Henry Merriman of Woodbury, Heminway Merriman, and William G. Merriman, both of Watertown, one daughter, Mrs. Guerin B. Carmody of Woodbury, and ten grandchildren.

J. Harold Root, Sr., m.d.

Joseph B. Kilbourn, M.D.
1887 - 1964

Dr. Joseph Birney Kilbourn of Simsbury, died of leukemia at the Hartford Hospital on May 10, 1964, at the age of 77. He was born in Hartford, where he attended public schools and was graduated from Trinity College. He studied Medicine at the College of Physicians and Surgeons in Baltimore, Maryland, where he received his M.D. degree in 1911. He served his internship at St. Vincent's Hospital in New York City. He pursued his preparation for surgery at the University of Vienna and returned to New York where he practiced surgery on the staff of Bellevue and German Hospitals, and the dispensary of Lenox Hill Hospital.

He returned to his home town and practiced in Hartford, where he decided to take up ophthalmology and he went to Austria for his special work in that department. On his return to Hartford, he became a member of the staff of Hartford Hospital, McCook Memorial Hospital and Cedarcrest Sanitarium. He took an active part in the Hartford Dispensary and also did special work at the Glaucoma Clinic.

Dr. Kilbourn had a most unusual experience, in that he was selected to organize and head the Royal Austrian Ambulance Train in World War I. He was decorated by Austria for outstanding work in this capacity on several fronts. He had a great ambition to help those in need and in World War II he was a member of the National Draft Board and President of the Friends of Austria, Inc., which helped refugees. For this latter work, he was cited by Pope Pius, XII.

It was not until he became interested, that the Eye Clinic was established at the Hartford Dispensary.

He was a member of the Connecticut Historical Society, the Sons of the American Revolution and the Antiquarium and Land Marks Society. He was also a member of the American Medical Association, the State, County and Hartford Medical Societies; and the Eye, Ear, Nose and Throat Society who had honored him by making him Past President of that organization.

Dr. Kilbourn married the former Baroness von Gussick, who survives him. They had two sons, O. Paul Kilbourn of San Francisco, Joseph B., Jr. of Simsbury and two daughters, Miss Josefa Kilbourn and Miss Christine Kilbourn of Simsbury.

Dr. Kilbourn's father was a physician and he had one brother, Austin Kilbourn, who is also a physician and lives in Hartford. His other brother, Orrin Kilbourn, lives in West Hartford and his sister, Mrs. Constance Payne lives in Providence, Rhode Island.

Joe Kilbourn was most energetic, thoughtful, kindly, loyal and a perfect gentleman who will be greatly missed by his family and all of his many friends.

Claude C. Kelly, m.d.

In Memoriam

Carwin, Joseph L.—Stamford; Meharry Medical College, Nashville, Tennessee, 1932. Dr. Carwin was a practicing physician in Stamford for 29 years. He was a staff member of both the Stamford Hospital and St. Joseph's Hospital, and a member of the courtesy staff at Greenwich Hospital. Dr. Carwin was a member of the Stamford Chapter, American Academy of General Practice, the American Medical Association, the Connecticut State Medical Society, the Fairfield County Medical Association, and the Stamford Medical Society. He was past president of the Fairfield County Medical Association, the Stamford Medical Society, the Stamford Chapter, American Academy of General Practice, and served two two-year terms as delegate to the House of Delegates of the Connecticut State Medical Society. In 1960, Dr. Carwin and his wife, Dr. Joyce Yerwood Carwin, visited the Soviet Union and European countries as members of a delegation from the National Medical Association. Dr. Carwin was also active in the work of many civic associations in Fairfield County. Dr. Carwin died June 30, at the age of 59.

Hewes, Carlisle T.—West Hartford; University of Vermont Medical School, 1931. Dr. Hewes was a retired physician and surgeon in Groton for 28 years. He was health officer for the community for 18 years and also served for seven years as a coroner's physician. Dr. Hewes was a member of the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. Dr. Hewes died July 1, at the age of 60.

Schaefer, Jacob—East Hartford; Tufts Medical School, 1917. Dr. Schaefer was a practicing physician in the Hartford area for the past forty years. He was a captain in the Army during World War I, and served as a major in World War II. Dr. Schaefer was on the staff of the Hartford, Mt. Sinai, and St. Francis hospitals. He was a member of the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. Dr. Schaefer died June 25, at the age of 70.

Wheatley, Louis F.—Brookfield, Vermont; Tufts Medical School, 1903. Dr. Wheatley was a pioneer in the development and use of the X-ray in the United States. For 20 years, from 1919 to 1938, Dr. Wheatley served as director of the X-ray department at Grace Hospital, New Haven. Upon leaving this position, Dr. Wheatley entered into private practice in New Haven.

Before coming to New Haven, Dr. Wheatley was a member of the surgical staff of Meriden Hospital, president of the Meriden Medical Society, and served as health officer of Meriden. In 1917, Dr. Wheatley entered World War I as a lieutenant at the Military School of Roentgenology in New York. He was later transferred to the U. S. Army General Hospital in Denver, where he developed the X-ray department. He was discharged from the Army in 1919, with the rank of captain. During World War II, he served as a major in the United States Army Reserve.

Dr. Wheatley was the author of numerous articles on X-ray diagnosis and treatment. He was a diplomate of the American Board of Radiology, a member of local and national Roentgen Societies, the American Medical Association, the Connecticut State Medical Society, and the New Haven County Medical Association. In 1950, Dr. Wheatley retired from practice and took up residence in Brookfield, Vermont. He died July 5, at the age of 87.

PLACEMENT OPPORTUNITIES

The Society's Placement Service is in receipt of the following:

Hartford County—WANTED—Senior physician for Veteran's Home & Hospital. License to practice medicine and surgery in Connecticut.

Hartford County—Internists practice available, excellent location, abundant free parking.

Hartford County—WANTED— part time psychiatrist in hospital.

Fairfield County—Long established medical practice and house for sale.

Fairfield County—WANTED—general practitioner or internist to take over physician practice, former occupant leaving to specialize.

New Haven County—WANTED—pediatrician.

OCCUPATIONAL PHYSICIAN for state employees' clinic located in Hartford. 35 hour week, 3 weeks vacation, up to 120 days sick leave, paid insurance program, social security and liberal retirement. Requires at least two years' general practice. Starting salary $11,640, going to $12,380 end of first year, then advancing $540 annually to maximum of $15,080. Reply directly to B. Dearington, State Department of Health, State Office Building.

1964 MEETINGS

September 25—39th Connecticut Clinical Congress, Mary S. Harkness Memorial Auditorium at Yale School of Medicine, New Haven.

October 29—181st Semi-Annual Meeting of the New Haven County Medical Association will be held on Thursday, October 29, 1964, at Waverly Inn, Cheshire, Connecticut.

BOOK REVIEWS

CLINICAL DISORDERS OF THE HEART BEAT by Samuel Bellet, M.D., Lea and Febiger, Philadelphia, Pennsylvania, 1963, 1105 pp. $28.00.

Reviewed by: LOUIS H. NAHUM

The first edition of this book came out in 1953. At this time it was considered to be "comprehensive, accurate, readable and profusely illustrated." This second edition is larger by over 700 pages and even the old chapters have been completely rewritten. This alone gives us a clue to what has happened to our knowledge of cardiology in the last ten years. But to get the real facts one must carefully go through this important new edition.

In the last ten years we have learned much about electrophysiology of the five different specialized cells of the heart. New knowledge has become available as to the causes, mechanisms and production of factors that precipitate arrhythmias. New improved diagnostic methods are with us such as continuous electrocardiographic monitoring during surgery, cardiac, catheterization, intravenous infusion of drugs. We now have knowledge of the site of action and how toxic effects are induced by antiarrhythmic drugs.

All this knowledge has become important especially because of the growing number of operations on the heart, often in poor risk patients. The recognition of arrhythmias and application of a particular type of therapy has assumed increasing importance. We now have new electronic devices for increasing cardiac rate in complete atrio-ventricular block, in the treatment of cardiac arrest and ventricular fibrillation.

New knowledge has appeared as regards arrhythmias in the fetus. We are clearer about the brain-heart relationship. There is a new recognition of the role of electrolytes in production of cardiac arrhythmias such as hypopotassemia and the use of sodium and potassium in treatment.

It is obvious a new edition was urgent and Dr. Bellet has succeeded again in making a comprehensive, accurate, readable and profusely illustrated book incorporating all the new knowledge. He obviously has kept in mind the interest of the student and internist as well as cardiologist in writing this book. There is a summary of the salient features and a glossary of terms. Each chapter terminated by references both most recent and those with greatest historical interest.

The book is divided into seven sections. The introduction offers anatomy, physiologic considerations and hemodynamics. Then came general considerations, discussion of individual arrhythmias, general diagnostic procedures, arrhythmias in certain clinical states, drug therapy. Finally "Other Procedures" in therapy such as carotid sinus pressure, artificial pace makers, defibrillations and cardioverters.

In a book such as this it might have helped to introduce a unifying concept of arrhythmias as they are related to the autonomic nervous system, the atrial flutter and fibrillation being promoted by acetyl choline and the tachycardias both atrial and ventricular promoted by epinephrin.

MARRIAGE COUNSELING IN MEDICAL PRACTICE. By Ethel M. Nash, M.D., Lucie Jessner, M.D., D. Wilfred Abse, M.D. Published by The University of North Carolina Press, Chapel Hill, N.C. 368 pp. $8.00.

Reviewed by: DENIS S. O'CONNOR

The tremendous changes in the diagnosis and treatment—and to be more accurate—in the elimination of disease entities in the past twenty-five years has not been accompanied by a corresponding change in emphasis in the medical curriculum. Each of the many specialties which have been accorded recognition in the curriculum has sought to enhance its importance in the amount of time devoted to its study with a resulting indigestability of the vast quantity of medical informaion available and yet with an insufficiency of teaching on some of the newer para-medical subjects which the general medical adviser sorely needs to meet the needs of the patients of today.

Because a doctor has spent years in the study of anatomy and physiology he is presumed to know much about techniques, as well as the disturbances of techniques. This is especially true in relation to the physiology and pathology of reproduction. Actually, the average physician probably is no more knowledgeable than the average man. But because he is a physician he is supposed to have the answers which his married patients bring to him.

This is one very important field in which his regular medical education has probably failed him because it is unusual to find a doctor, at least in his early years of practice, who is equipped to give sound advice to his married patient who brings to him his difficulties in adjusting to marital life.

There is a large volume of material on all phases of sex life on the market today but it is difficult to find a book which is written in non-technical language and yet in such a scientific approach that the average busy doctor can read, understand and digest for practical application.

"Marriage Counseling in Medical Practice" is such a book. Except for Chapter XV which is not essential to the subject, this book is easily readable and most helpful in understanding the problems, the solution to which can be the salvation of an otherwise disastrous marriage.

The practicing general practitioner, the gynecologist and the psychiatrist who may feel insecure in advising on marital problems could find this book a welcome aid. The medical student could with profit take the short time necessary to read this book and would doubtless add it to his library. The social worker and others who have to deal with the problems of sex life in marriage would be well advised to have this volume at hand for reference when faced with a difficult problem. It cannot be recommended too highly.

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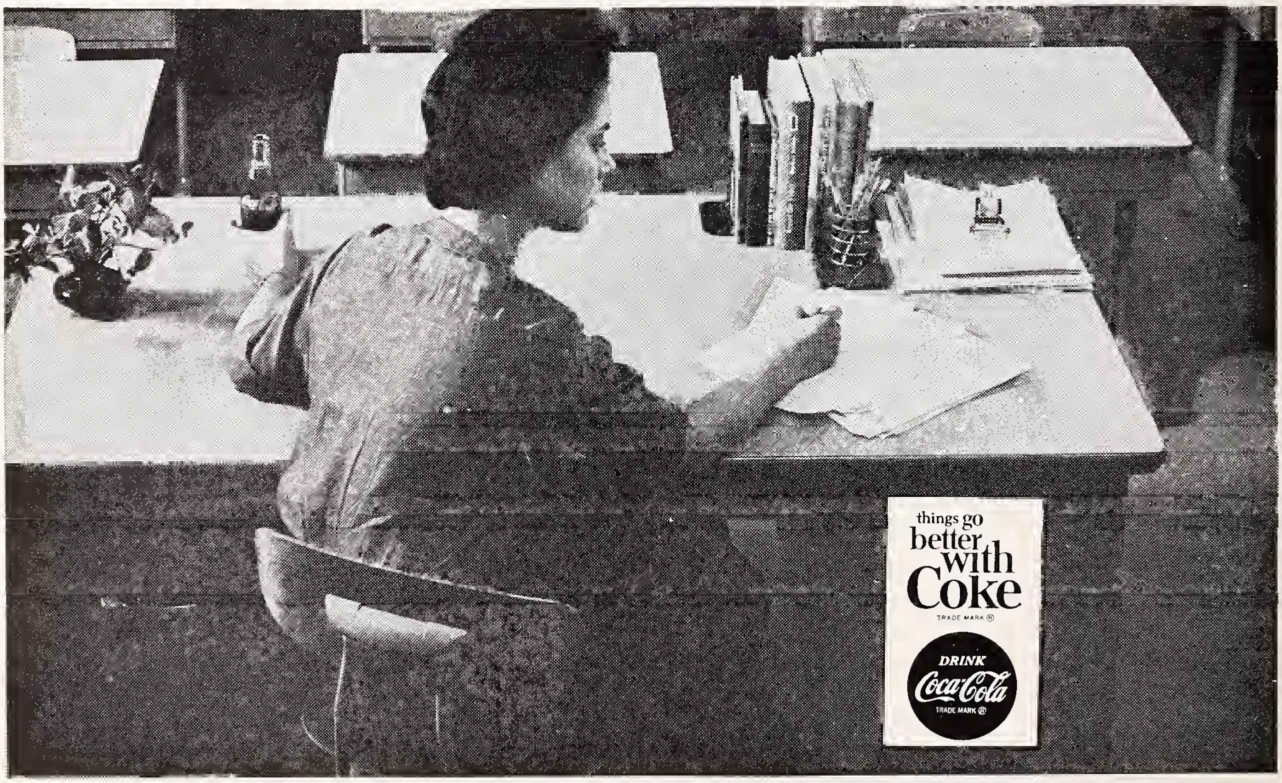

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APPRAISAL OF CURRENT CONCEPTS IN ANESTHESIOLOGY.

Reviewed by: FRANCIS KIVLAHAN

In this, the second volume of Current Concepts, Dr. John Adriani and his twenty-one contributors have covered a wide range of subjects. The 468 pages are divided into 45 chapters, and aimed, as stated in the Preface, toward trainees and specialists in Anesthesiology in strictly clinical practice.

While relatively little space has been given to specific details, since this is available from many other sources, the editor has succeeded in accumulating a wealth of information, the importance of which cannot be questioned. To cover all aspects allied to present-day Anesthesia would require many volumes. The editor must be complimented for his lucid, concise presentation, accompanied by an adequate list of references for each chapter.

The book does not represent a mere collection of synopses of current literature, but rather a clinical and thorough evaluation of various subjects. Each subject contains not only an introduction with historical and physiological and pharmacological background, but also a fairly completely documented discussion and a concise Summary. Verbosity is minimal. Most emphasis has been placed on Endocrine matters, to which 8 excellent chapters are devoted. Other less fashionable topics such as Mongolism, Xenon anesthesia, Intra-Ocular tension, and Hepatic Coma have also been presented. The final chapter on statistics is particularly noteworthy, because it is a rather clear, brief, complete and timely evaluation of a subject rarely seen in an Anesthesiology text or monograph. The discussion on Blood Transfusion, although rather limited in space, is worthy of special mention.

The author of the chapter on "Antianalgesic Drugs" is in error in his statement that Dundee uses the method of Von Frey. Actually, his technique is similar to that of Clutton-Brock. Unfortunately, the book is devoid of illustrations. It, however, is produced in print easy to read and priced at $10.75. Dr. Adriani and his fellow-contributors emphasize the fact that the prime reason of the book is the aid and enlightenment of the clinical anesthesiologists and trainees in anesthesia.

CASE STUDIES IN OBSTETRICS AND GYNECOLOGY by F. Jackson Stoddard, M.D., W. B. Saunders Company, Philadelphia and London, 1964, 299 pp. $8.50.

Reviewed by JAMES R. CULLEN

This is a very excellent book and, as may be seen by its title, concerns itself with case studies presented in a clear and interesting manner with related discussion and questions and answers. There are also many fine illustrations and diagrams throughout this text.

The author is a member of the third generation of well-known physicians. His ancestors learned the practice of medicine by methods described in this book, since case studies were the usual method of teaching prior to 1925.

Twenty-two chapters composed of actual cases under the following titles make a most interesting work. These are: Amenorrhea, Disturbances of Menstruation, Endometriosis, Infertility, Ectopic Pregnancy, Abortion, Placental Disorders, Medical Disorders, Hematologic Disorders, Urinary Tract Disorders, Emotional Aspects, Toxemia of Pregnancy, Post-partum Hemorrhage, Complications of Labor, Obstetrical Complications, Relaxed Pelvic Floor, Vulva, Vagina, Cervix, Uterus, Ovary, and Fallopian Tube.

Cases as seen in actual practice and consultation relative to the disease headings above are discussed under the sub-headings of: Testicular Feminization, Adrenal Virilism, Abnormal Uterine Bleeding, Premenstrual Tension, Septic Abortion with Shock, Abruptio Placentae, Heart Disease in Pregnancy, Faulty Hemostatic Mechanisms, Frigidity and Dyspareunia, Prolapsed Umbilical Cord, Prolonged Labor, Appendicitis in Pregnancy, Obstetrical Anesthetic Accident, Vaginitis in Children, Benign Lesions of the Cervix, Late Carcinoma of the Cervix, Ovarian Tumor: Benign and Malignant, and Pelvic Inflammatory Disease.

The practical aspects of genetics, embryology and reproductive physiology are presented clearly and interestingly as the author tells the clinical history and then discusses the pertinent facts, pointing the way to a precise diagnosis and needed treatment with elimination of non-essentials.

The author implies in his preface that too many ward rounds are made in the conference room instead of at the bedside and he attempts to show the need for a return of the physician to the patient. In writing this book, he hopes to achieve certain objectives, namely to:

1. Integrate the basic sciences and related clinical specialties by means of a typical illustrative case.
2. Help the student or clinician screen the important from the unimportant aspects of a case and by so doing restrain him from ordering unnecessary laboratory procedures or using drugs which are inappropriate though highly advertised.
3. Make the reader a better consultant or give him a better understanding of problems confronting the consultant.
4. Avoid a stereotyped approach to management by showing how a particular patient's problems differ from those of other patients; for example, to indicate what treatment would have been used if the patient were forty-five instead of twenty-five years old.
5. Describe and discuss some unusual cases such as diabetes in pregnancy or gonadal dysgenesis which students may never see during medical school days and practitioners may see so rarely that they may fail to recognize them or manage them correctly.
6. Help the reader prepare case presentations which are concise, pertinent and interesting to most listeners.
7. Challenge some readers to probe further into unknown aspects of a given case.
8. Keep the tired physician awake a little longer than a textbook or medical journal does. It is my belief that reading about a patient is more interesting and stimulating than reading about a disease.

On the whole, I believe he has succeeded very nicely in accomplishing his desire.

This book reminds one of the famous Massachusetts General Hospital Case Studies, which many readers will remember. The problems dealing with interesting endocrine cases are most unusual. The reviewer enjoyed reading this particular book, since it covers about all obstetrical and gynecological problems and strongly recommends it to students, physicians, interns, endocrinologists, and specialists interested in the field of obstetrics and gynecology.

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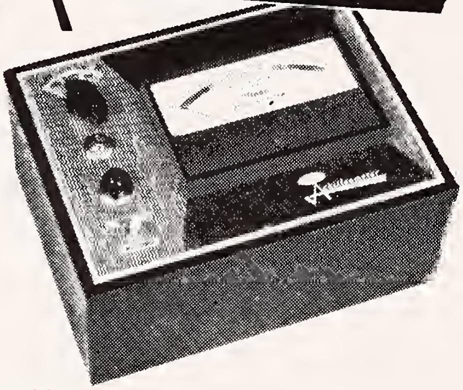

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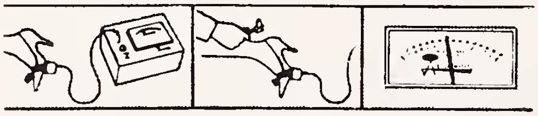

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A SAVAGE PLACE. By Frank G. Slaughter. Published by Doubleday and Co., Inc., 575 Madison Avenue, New York 22, New York. 248 pp., $4.50.

Reviewed by: DENIS S. O'CONNOR

This small novel is not likely to become one of the outstanding works of fiction of this year. It is an entertaining novel of an Eastern industrial community that was dying with the decadence of the family controlled industry on which so frequently the part of a town depended for its life.

The story of the strangle hold of the psychotic family on the rebirth of the town, the key role of the brilliant young surgeon from the other side of the tracks, the struggle to change a selfishly operated and inadequate hospital into an accreditated institution is interspersed by the usual romantic attachments which are the indispensable ingredients of the novel.

It can be recommended for light reading with special interest for the doctor who may see in the hospital aspects of the story some of the problems which have faced him on his own balliwick.

CURRENT PEDIATRIC THERAPY by Sydney S. Gellis M.D., and Benjamin M. Kagan, M.D., W. B. Saunders Company, Philadelphia, Pennsylvania, 1964, 747 pp. $16.00.

Reviewed by: LOUIS H. NAHUM

Here is the book that should be on the desk on every physician who at times has responsibilinty for treating the child. For here will be found the best methods of treating all ills that befall the child from the experience of two hundred and forty-eight outstanding contributors. They are not all pediatricians, for some are surgeons like Lillehei. Some are gastroenterologists, like the celebrated Burrill Crohn. Some are geneticists and some are toxicologists, and some are experts in infectious diseases. The pediatricians are all men of great wisdom and experience, many of them chiefs of pediatric departments in the great medical schools of this country.

There is great need for such a work, since therapeutics has been advancing on a broad front this past decade. The articles are short, to the point, and complete. The editors are to be commended for the vast array of talent they were able to assemble and the publishers deserve commendation for the two column format and easy readability of the text.

The book does not contain diagnosis and etiology, except as the latter is woven into the logic of therapy. This is justifiable because description of disease, differential diagnosis, and etiology should be sought for in many available texts devoted to this purpose.

The editors of this excellent manual of current pediatric therapy are well known as teachers and practitioners of pediatrics. Dr. Gellis is professor of pediatrics and chairman of the department of pediatrics, Boston University School of Medicine. Dr. Kagan is clinical professor of pediatrics of U.C.L.A.

MEDICINE AND THE STATE by Matthew J. Lynch, M.D., and Stanley S. Raphael, M.B., Charles C. Thomas, Springfield, Illinois, 1963, 449 pp., $9.75.

Reviewed by: LOUIS H. NAHUM

The authors start with the following assumption: that mankind has an unquenchable thirst for freedom and justice. They have, therefore, collected, analyzed and arranged factual material from many countries to see whether socialized medicine satisfies man's unquenchable thirst for freedom and justice. England, Sweden, the USSR, Germany, Austria, New Zealand and Australia are studied from the standpoint of the history, evolution, and performance of national medical schemes.

In appraising the results of state medicine, the authors, both practicing physicians, have examined these from the point of view of the effect on the patient, the health of society, the medical profession, national economics, pattern of utilization of medical, hospital, and pharmaceutical services, and the incidence of sickness. From the start they point out that there is no parallel between public health and personal health care, the former is not concerned with the individual person, the latter is.

The authors believe that there is an insoluble conflict on the part of the physician in government controlled schemes of health. The physician must trust all his patients if he is to act his true role. At the same time he must mistrust and suspect every patient in order to protect the solvency of he scheme. There resuls curtailment of individual freedoms of both doctors and patients. Some think this infringement is justified by the argument that this is more of the nature of curbing willful freedoms, anti-social tendencies and selfish living. But what do we really find? What are the facts? There is a limitation of freedom and justice, there is coercion and restriction of voluntary effort towards self betterment. All the systems seem to commit its citizens to "mental and fiscal imprisonment." All the systems eliminate opportunity and challenge, and leave only the boredom of a limited certainty.

Sigerist has stated "Man has a right to health, is entitled to having this health secured—everybody, rich and poor, should have all the medical care that science can give." The authors' analysis of the schemes used by government to achieve these aims reveals state medicine as a failure.

Without doubt their conclusions will be challenged by Ministers of Health in the various countries. But the material they marshal deserves careful and objective study, especially by American physicians, who are fighting hard to guard their collective and individual member's freedom against encroachment of the state.

AN ATLAS OF CONGENITAL HEART DISEASE by Frank E. Sherman, M.D., Lea and Febiger Co., Philadelphia, Pennsylvania, 1963, 303 pp. $15.00.

Reviewed by: LOUIS H. NAHUM

In 1936 Maude Abbott assembled cases for her atlas of congenital heart disease. At this time the collected data was only of academic interest, since nothing could be done to correct any of the defects. Now pathologists, cardiologists and surgeons are joined to clarify, diagnose and treat congenital malformations. There are still a large number of cases that defy accurate and complete antimortem diagnosis and an even larger number which are presently incorrectable surgically. Perhaps to decrease this number is one of the principal justifications for assembling this atlas.

It is evident that Dr. Sherman in planning this study was highly motivated with the aim of diagnosis and surgical treatment. The way he presents his material and the discussion which follows suggests he is one of a surgical team. The technique he has used in his postmortem examination is calculated to be of benefit to the surgeon. He examined the

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heart in situ without removing it until the diagnosis is clear. In this way, it is possible to diagnose venous and other anomalities. It allows the cardiologist to visualize the condition and its projection as he sees it in the X-ray. He is able to correlate the electrocardiogram with the geometry of the heart. Finally, the surgeon can visualize the heart in the same position as he will encounter it at operation.

The atlas contains a detailed study of the gross anatomic observations made on 503 autopsy specimens of the heart museum at Children's Hospital in Pittsburgh. But it is more than a simple statement of morphology of classified lesions of the heart. It also contains notes on embryology, pertinent clinical information as well as simple case reports of rare lesions. The author has gone further. Mechanics are noted to allow correlation of morphology and function. Beside all this, it is a quick reference for specific anatomic lesions as well as furnishing an excellent bibliography.

Since 1954 the author has been assembling and organizing the cases of congenital heart disease into a valuable museum. The atlas now makes this valuable material available everywhere.

The publishers are to be congratulated on a beautiful printing job and excellent reproduction of illustrations. The book is a must for students of heart disease and surgeons that work to correct cardiac defects.

Special Notices

SEMINAR TREATMENT OF COMPLETE HEART BLOCK

October 10 and 11, 1964

On October 10 and 11, 1964, a Seminar on the Treatment of Complete Heart Block, sponsored by the Vermont Heart Association and the University of Vermont College of Medicine will be held at the DeGoesbriand Memorial Hospital, Burlington, Vermont. In addition to the regular members of this College, Samuel Bellet, M.D. (or co-worker), William M. Chardack, M.D., Gordon K. Moe, M.D. and Paul M. Zoll, M.D. have agreed to participate as guest speakers. Further information can be obtained from Eugene Lepeschkin, M.D., Cardiovascular Research Unit, DeGoesbriand Memorial Hospital, Burlington, Vermont.

AMERICAN COLLEGE OF NUTRITION

October 25, 1964

The annual scientific meeting of the American College of Nutrition will be held at the Americana Hotel in New York City on Sunday, October 25, 1964 at 9 a.m. For further information, please contact Robert A. Peterman, M.D., F.A.C.N., Secretary-Treasurer, 3 Craig Court, Totowa Boro, New Jersey, 07512.

SECOND NATIONAL CONFERENCE ON CARDIOVASCULAR DISEASES WASHINGTON, D.C.

November 22-24

The Nation's leading authorities in heart disease research, prevention, treatment, rehabilitation and education will meet in Washington, D.C. for the Second National Conference on Cardiovascular Diseases, November 22-24 (1964).

The Conference is being co-sponsored by the American Heart Association, National Heart Institute, and the Heart Disease Control Program of the U.S. Public Health Service. Originally planned for January 1965, "the earlier date will permit the results of the Conference to be coordinated with the recently announced President's Commission on Heart Disease, Cancer and Stroke, in preparing a report requested by President Johnson," say Conference Chairmen, Dr. Carleton B. Chapman, President-elect of the American Heart Association, and Dr. Ralph E. Knutti, Director of the National Heart Institute.

Among those attending the Conference from the Hartford Area are: Paul H. Twaddle, M.D., of Wethersfield, President of the Connecticut Heart Association; Henry Eisenberg, M.D., and William J. Lahey, M.D., both of West Hartford; and Nicholas J. Lavnikevich, and Horace A. Brown, both of Simsbury.

Among others attending from Connecticut are: Drs. Roy Acheson, Alvan R. Feinstein, Averill A. Liebow, Harold M. Marvin, Ruth Whittemore, all of New Haven, and Miss Audrey McCluskey, of Hamden.

At the Conference, more than 500 invited experts will review and discuss advance reports of more than 400 scientists, who have been at work for more than a year developing summaries and interpretations of developments in the cardiovascular field since 1950, date of the first national conference.

Additional information and recommendations arising from these discussions will then be incorporated in the Conference report.

All the disease entities in the cardiovascular field will be reviewed, including coronary heart disease, high blood pressure, stroke, rheumatic fever and rheumatic heart disease, inborn defects of the circulatory system, among others. Particular attention will be paid to developing recommendations concerning research, unmet needs in professional and public education, and methods for making extensive use of existing medical and public health techniques.

The specific objectives of the Conference are:

To examine the cost of cardiovascular disease in terms of their burden on human, financial and social resources; to focus on the advances made since 1950; to report on the present status of knowledge of cardiovascular diseases and on the application of this knowledge at the community level; to project to opportunities and future needs in research, training and the application of knowledge; and to assist physicians, other health personnel and the public in useful and wider application of current knowledge through publications and dissemination of the results of the Conference.

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BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Physical Examination of the Surgical Patient. By J. Englebert Dunphy, M.D., F.A.C.S. and Thomas W. Botsford, M.D., F.A.C.S., W. B. Saunders Company, Philadelphia and London, 1964. Third Edition. 396 pp. Illustrated. $8.50.

The Liver and Portal Hypertension. By Charles G. Child, 3rd, M.D., Volume 1 in the Series Major Problems in Clinical Surgery, J. Englebert Dunphy, M.D., Consulting Editor. W. B. Saunders Company, Philadelphia and London, 1964. 231 pp. Illustrated. $8.50.

Christopher's Textbook of Surgery. Edited by Loyal Davis, M.D. W. B. Saunders Company, Philadelphia and London, 1964. Eighth Edition. 1481 pp. 1341 Illustrations and 744 Figures. $18.50.

Atlas of General Surgery. By Joseph R. Wilder, M.D., F.A.C.S. Second Edition. The C. V. Mosby Company, St. Louis, Missouri, 1964. 317 pp. Illustrated by Shirley Baty. $23.50.

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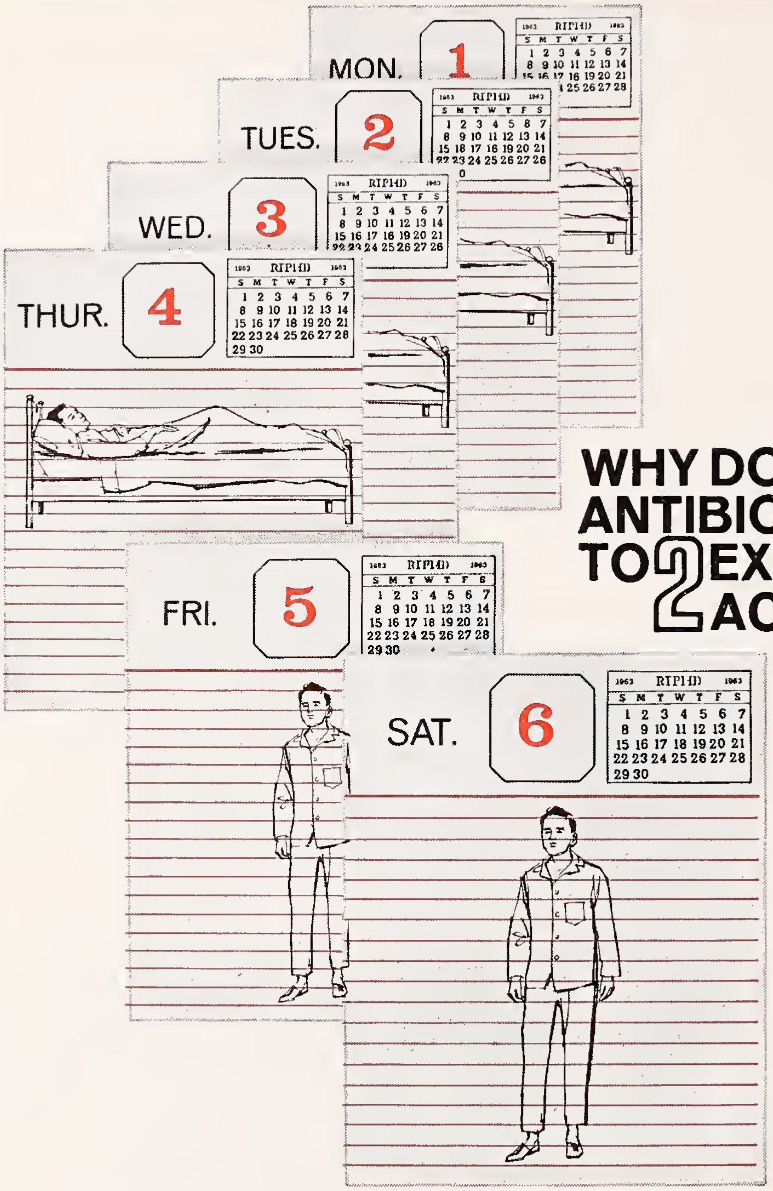

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AMA Issues Smoking Pamphlet In Information Campaign

The American Medical Association, in a new pamphlet on "Smoking: Facts You Should Know," pointed out recently that most authorities agree that, from the health standpoint, it is preferable not to smoke.

"To smoke or not to smoke is, of course, a matter of individual choice," the AMA said.

"Certainly, if you haven't started the habit, you should carefully consider all the facts concerning your future health before doing so," the medical organization advised.

The pamphlet will be used in the organization's continuing nationwide campaign to inform young people on health hazards of tobacco. The educational drive among young people was adopted as official AMA policy by the association's House of Delegates at its annual meeting in June, 1963, at Atlantic City.

"People who smoke usually realize that their habit is costly and often is a threat to life," the AMA pamphlet says. "Numerous deaths occur each year from burns and suffocation due to falling asleep while smoking. To this, add forest fires and explosions when cigarettes are lit in the wrong place at the wrong time. To the cost of cigarettes, add the cost of repairing marred furniture, burned sofas and rugs, and holes in clothing. And finally, add the possible damage to a priceless possession—your health.

"Skilled research personnel say that tobacco smoking, and particularly cigarette smoking, shortens life expectancy. It is alleged to cause cancer of the lungs and bladder, increase the frequency of such circulatory diseases as coronary heart disease, heart muscle damage, arterial disease, and possibly high blood pressure. It contributes to chronic bronchitis, emphysema, and to other obstructive lung diseases, and is related to a host of other health problems. It reduces the oxygen-carrying ability of the blood. Physicians and researchers who believe these observations to be correct say, 'Don't smoke! If you do smoke, quit. If you don't smoke, don't start.'

"Some equally competent physicians and research personnel are less sure of the effect of cigarette smoking on health. They believe the increase in these diseases can be explained by other factors in our complex environment. They advise "Smoke if you feel you should, but be moderate."

"An individual can try to reach a solution to his own smoking problem by studying the evidence, making a rational decision, and acting on it.

"Smoke, a product of combustion, is a mixture of gases, various vaporized chemicals, and millions of minute particles of ash and other solids. These are drawn into the nose, throat, and lungs during smoking. The smoke includes some vaporized nicotine, a toxic substance found in tobacco, although much of it is destroyed by heat. It contains tars and other products from the partial burning and distillation of the tobacco.

"Both the nicotine and the tars are partly deposited onto the cold portion of tobacco between the point of combustion and the mouth, only to be revaporized when the fire reaches them. Thus, a smoker gets more nicotine and tar if he smokes to a short butt. A significant amount of carbon monoxide is also produced which is quickly picked up by the oxygen-carrying hemoglobin of the blood and blocks its oxygen-carrying ability. Drawing air through burning tobacco reduces the oxygen content of this air since combustion converts much of the oxygen into a carbon dioxide and carbon monoxide.

"As smoke is drawn into the breathing passages and the air sacs of the lungs, the cooling of the smoke permits vaporized chemicals to settle onto the surrounding membranes. The point of greater concentration is where a large airtube divides into two smaller ones. Interestingly, this point of division is where most lung cancer begins.

"Pathologists, physicians skilled in the microscopic anatomy of disease, consistently find that the lining membranes of the air passages of smokers are thickened. The hairline cilia on these membranes become damaged and are less effective in removing the toxic and irritating chemicals introduced by inhalation of smoke.

"Pathologists also have found that smoking not only thickens the lining membranes of the air passages and obstructs them with secretions, but also stimulates a contraction of the muscles in the air passage walls which narrows them and further reduces air flow. The increased effort used to exhale breaks down the delicate walls of the air sacs and may ultimately lead to emphysema, a disabling lung disease. There is considerable evidence that a single cigarette will markedly reduce the air flow of even an experienced smoker.

"Smoke also affects the membranes lining the larynx or voice box. A pathologist identifies a smoker's larynx by the thicker, often swollen vocal cords. The changes in the voice box are similar to those that occur in the air passages and in the lungs.

These irritations cause swelling and increased secretion and result in smoker's cough, which, in turn, breaks the walls of the finer air sacs and contributes to emphysema.

"Smoking affects the heart and blood vessels. Nicotine, if injected or taken in tobacco smoke, stimulates that part of the nervous system that controls the heart, blood vessels, and other internal organs that function almost automatically. For years, smoking has been known to be related to Buerger's disease, a constriction of the small arteries in the hands and feet that can lead to gangrene and necessitate amputation. So-called tobacco heart or tobacco angina is a combination of chest discomfort, fast heart beat, extra heart beats, and shortness of breath which disappear when a person quits smoking. Smokers also have a higher death rate from coronary heart disease than do nonsmokers.

"Among other effects of smoking are those of an apparent tobacco allergy in some sensitive persons, aggravation of gastric ulcers, and a form of blindness called tobacco amblyopia. Patients with these conditions are almost always advised not to smoke.

"While all tobacco smoking affects health and life expectancy, cigarette smoking appears to have a much greater effect than smoking cigars and pipes. Among the reasons offered is that cigar and pipe smokers often do not inhale and that the smoke, traveling farther, is cooler and less irritating when it reaches the mouth.

"Filters and denicotinization of tobacco in cigarettes are alleged to reduce the hazards. However, denicotinization has no effect on the kind or amount of tar in the smoke.

"That smoking is related to psychological and social situations is well known not only in the reasons people give for smoking, but also in other obvious reasons which they don't give. Young people often start smoking in imitation of older people who smoke or as an expression of a subconscious wish to be like them. Older children and youth want to be accepted by their friends and associates. Often friends dress alike, talk alike, and have other behavior in common. Smoking may be part of this attempt to conform. Not smoking could also be part of a group pattern.

"As a means of relaxation, the mechanical aspects of smoking are recognized. Under tension or during an awkward lull in activity, smokers probably do relax by taking out a package of cigarettes, choosing one, getting matches, lighting the cigarette, and handling it.

"Some authorities suggest that a cigarette represents a reward that a smoker can offer himself whenever he wishes, or that the act of smoking represents a means of self-expression. In young people, it may represent freedom to do as one pleases, or be an act of rebelliousness against adult authority. Other authorities believe that people smoke because of the need for oral activity to fulfill an unsatisfied suckling reflex.

"Recent studies have shown that youngsters whose parents smoke will also tend to smoke. If older brothers and sisters smoke, the younger ones are more likely to become smokers.

"Physicians, other scientists and many health agencies have studied the relationship of smoking to health and most are in general accord.

"The most extensive examination of smoking was published in January, 1964, by the Advisory Committee to the Surgeon General of the U.S. Public Health Service. The Committee reported that the magnitude of the effect of cigarette smoking far outweighs all other factors in relation to lung cancer in men. Although the data for women are less extensive, they point in the same direction.

"The longer you smoke and the more you smoke, the greater the risk of developing lung cancer. If you quit smoking, the risk is diminished.

"Pipe smokers run more of a risk of developing lung cancer than nonsmokers, but much less risk than cigarette smokers.

"Cigarette smoking is also a significant factor in laryngeal cancer in men. It is the most important cause of chronic bronchitis in the United States and is closely related to pulmonary emphysema. Coughing, spitting, or both are more frequent among cigarette smokers than among nonsmokers.

"Manufacturers are trying to reduce the hazards of smoking by modifying tobacco, reducing nicotine content, and filtering the tars. It seems that to be safe, tobacco smoke must be reduced to warm air.

"Research has been initiated to find and isolate or refine harmful substances so that those who smoke may continue to smoke safely. Thus far, the results have been discouraging and an early breakthrough is unilkely. However, the American Medical Association is sponsoring a large-scale study to determine what human ailments may be caused or aggravated by smoking, what elements in smoke may be harmful, and how these can be eliminated.

"Most authorities agree that evidence, statistical or otherwise, is accumulating which indicates the desirability for the heavy smoker to cut down the smoking habit to the point of moderation. Medications are being sold which are intended to keep the smokers from smoking. Unfortunately, these have not been successful. Anti-smoking clinics are being continually developed and may help many smokers. "If you haven't started the habit, you should carefully consider all the facts concerning your future health before doing so."

Swimming Safety

The summer swimming season is here again. If past averages hold, somewhat more than 6,000 Americans will drown. Most of these drownings could be avoided.

The basic rules of water safety should be well known to everyone old enough to read; they are repeated each season by health and safety organizations throughout the nation. And yet most drownings occur when someone has violated one of the safety rules.

These are the fundamentals—Never swim alone: Don't swim just after eating or when overly tired; Don't overestimate your ability and endurance; Swim at protected pools or beaches under the supervision of a trained lifeguard; If a boat overturns stay with it and don't try to swim a long distance to shore; Never dive into unknown waters.

Know about artificial respiration and how to apply it. The mouth-to-mouth method is explained in the First Aid Manual of the American Medical Association. It's not very difficult—Start immediately, the victim can survive without oxygen to the brain for only a few minutes; Put the victim on his back, pull the chin well up, make certain the windpipe is clear; Put your mouth over the victim's mouth, pinch shut his nose, and blow hard; Repeat 12 to 15 times per minute; Keep it up until medical help arrives.

Skin diving and SCUBA diving are fine sports that are drawing more enthusiasts each season. Both require special training and knowledge and good physical condition. If you plan to be a diver, take a course in underwater survival. And get yourself into good physical training for strong swimming.

Water skiing is another exhilarating sport, but it also has hazards. The man handling the boat should know what he's doing. The skier should always wear a life jacket. Even a strong swimmer can be winded by a hard fall at high speed.

Private pools are gaining rapid favor in the United States. If you have a pool, or use a neighbor's, there are certain safety fundamentals—Is the pool kept clean and the water chemically purified? Walk, don't run, about the pool, and be careful with horseplay; Fence the pool and keep the gate locked to keep out small children; Keep rescue equipment such as long poles and ring buoys handy; Keep bottles and glasses away from the concrete pool deck.

Are all in your family or household good swimmers? If not, arrange lessons at the Y.M.C.A. or somewhere else in which qualified instructors conduct classes. Many drownings occur among nonswimmers or weak swimmers. A refresher course even for good swimmers might save a life by helping the swimmer to get into better physical condition.

A final thought—If you get into trouble in the water, *don't panic.* Keep your head, float on your back and paddle gently. It's possible to stay afloat for hours, if you don't panic and thresh out wildly.

Screening Test Described For Undetected Kidney Disease

A simple, sensitive screening test for spotting unsuspected kidney disease was described today by Boston researchers in the current *Journal of the American Medical Association.*

The telltale sign of kidney disease is increased activity of the enzyme lactic dehydrogenase (LDH) determined by urinalysis, according to the report by Drs. Warren E. C. Wacker, Lionel E. Dorfman and Elias Amador.

In most patients with potentially fatal kidney diseases the urinary LDH activity is significantly elevated, they said.

The most common kidney disease is chronic pyelonephritis, the authors pointed out. However, despite its prevalence, the disease remains undetected in 75 to 80 per cent of cases because symptoms are lacking or unusual, plus the fact that a definite laboratory sign often appears only intermittently, they said.

Therefore, progressive kidney failure too frequently results from a disease potentially amenable to drug therapy or surgery, they stressed.

Since LDH activity is elevated before symptoms appear, the test permits diagnosis and treatment of the disease before severe kidney damage occurs, they added.

In a study of 90 patients it was found that elevations of LDH activity correlated well with the severity of the disease.

LDH activity also proved to be consistently normal in benign high blood pressure but raised in patients with high blood pressure resulting from kidney diseases. For this reason, the authors said, the LDH measurement should be particularly useful in distinguishing one type of disease from the other.

The test could be used to detect progressive kidney disease which often complicates diabetes and could lead to better management of these patients, they added.

The three physicians, affiliated with Harvard Medical School and Peter Bent Brigham Hospital, previously reported that the LDH activity level could be used as a screening test for malignant tumors of the urinary tract.

Fatal Heart Attack Rate Low In U.S.-Italian Community

In the Italian community of Roseto, Pa., the rate of fatal heart attacks is "strikingly low" compared with four surrounding towns, a medical research team reported today.

The reason for the Rosetans good fortunte "is not clear at the present moment," Drs. Clarke Stout, Jerry Morrow, Edward N. Brandt Jr. and Stewart Wolf, Oklahoma City, wrote in the current *Journal of the American Medical Association.*

"The most striking feature of Roseto was the way in which the people seemed to enjoy life," the authors said in describing the 1,630 residents.

Ninety-five per cent of the population are first, second or third generation Italians. They are "gay, boisterous and unpretentious." The community essentially is a one-class, peasant-type society made up of simple, warm and very hospitable people. There is poverty, but no real want.

Surprisingly, in view of the low fatal heat attack rate, the researchers observed that the Rosetans eat a great deal and drink considerable alcohol, mainly wine. The impression also was gained that they consume substantially more calories and substantially more fat than the average American. Both men and women over age 21 were found to be overweight.

Whether the Rosetans' way of life contributes to their health is still to be determined, the researchers said. Genetic and ethnic factors may be important, they added, although deaths from heart attacks at relatively young ages have been documented among men born in Roseto but who lived most of their lives elsewhere in neighboring Pennsylvania, New York, or New Jersey.

The adults of Roseto have been interviewed, examined and tested in an effort to determine whether low death rate from heart attacks was matched by a low incidence of the disease and by relative longevity among the men. The results of these studies will be reported later, the researchers said.

The other communities surveyed along with Roseto during a seven-year period from 1955 through 1961 were Nazareth, Pa., population 6,209, predominantly German; Bangor, Pa., population 5,766, a mixture of several ethnic types including many Germans and Italians; Stroudsburg, Pa., population 6,070, and East Stroudsburg, Pa., population 7,674, both composed of mixed ethnic groups.

When the number of deaths from heart attacks were compared by town for the seven-year period, the only meaningful difference was between Roseto and the other four communities. The rate for Roseto was less than one-half that of Bangor, only one mile away.

The lower death rate on Roseto was particularly marked among men. Population figures revealed that of the five towns only in Roseto were there more men than women alive over the age of 55.

There were no deaths due to heart attacks of either sex under age 47 recorded during the seven-year period in Roseto.

The death rate per 100,000 per year from heart attacks in Roseto was 91 for men and 66 for women compared with 406 for men and 197 for women in Nazareth; 369 for men and 244 for women in Bangor; 439 for men and 132 for women in Stroudsburg, and 311 for men and 94 for women in East Stroudsburg.

Roseto was settled in 1882 by immigrants from Roseto, Valfortore, in the province of Foggia, Italy, according to the Journal report, Originally, most of the Rosetan men worked in the neighboring slate quarries. Today, most of the women and some of the men either own or work in small factories that manufacture shirts and blouses. Other men work in nearby steel mills and electrical industries, while only a few still work in the quarries.

Similar studies of coronary artery disease in various ethnic groups have yielded a variety of interpretations, the researchers pointed out.

Whatever the relevant factors, they said, it is evident that differences in the incidence of coronary heart disease do exist among different ethnic groups as well as among ethnically similar groups in different localities.

The Pennsylvania study was undertaken in an effort to minimize some of the variables inherent in a study involving widely differing geographical areas, they explained.

The authors are affiliated with the University of Oklahoma Medical Center and the Oklahoma Medical Research Foundation. Drs. Stout, Morrow and Wolf are in the neurocardiology research program of the department of medicine. Dr. Brandt is with the biostatistical unit and medical research computer center of the department of preventive medicine and public health.

Human Pesticide Storage Not Increasing

Retention of ingested pesticides in the general population has not increased since 1951, a study showed recently.

To investigate the nature and extent of the storage of chlorinated pesticides in human fat, Drs. William S. Hoffman, William I. Fishbein and Morten B. Andelman, Chicago, analyzed fat specimens obtained at autopsy from 282 persons.

Traces of pesticides on vegetables, fruits, and forage material may be eaten either directly by man or by animals that are in turn consumed by man, the researchers wrote in the current *Journal of the American Medical Association.*

Since chlorine-containing pesticides were more likely to be retained in human fat, about 20 were extracted and analyzed, they explained. However, only two, lindane and DDT, were found consistently in the samples, they reported.

Fear Underlies Habituation To Cigarette Smoking

Fear underlies tobacco habituation, according to Dr. Richard D. Chessick, a Chicago psychiatrist.

Persons habituated to cigarette smoking are seeking a "keyed up" state to protect them against the deep fear that they will be destroyed, ruined, or exposed if they let their ego defenses down, Dr. Chessick wrote in the current *Journal of the American Medical Association.*

In this sense, he said, tobacco habituation can be understood as an ego operation which constantly, through artificial means, keeps the ego functioning at a high level of alertness. The desperate psychic need and chronic pressure to maintain defensive mechanisms working continuously in high gear is the "essential psychic ingredient for many addictions and habituations," he pointed out.

This hypothesis is consistent with studies indicating that smokers tend to live faster and more intensely and to be more socially outgoing, the "counter phobic" aspects of which are obvious, Dr. Chessick commented.

The theory also is consistent with the fact that the compulsion to smoke in increasing amounts represents an ominous sign, he added.

"The lack of stabilization with a fairly constant amount of given addictive or habituating substance indicates that the function of the addiction or habit is not being fulfilled and sooner or later further steps will have to be taken by the ego to protect against the feared exposure or destruction," he said.

Patients who smoke in increasingly large amounts and are forced to stop are faced with the original threats that they have been trying to defend against, Dr. Chessick continued. Turning to food seems to be one of the characteristic ways of dealing with the unconscious problem, he said, and compulsive overeating becomes a substitute for the smoking habit.

Significant emotional disturbances may occur in persons who are not able to find satisfactory substitutes for smoking, Dr. Chessick warned.

Dr. Chessick is chief of the psychiatry service at Veterans Administration Research Hospital and assistant professor in the department of neurology and psychiatry at Northwestern University Medical School.

Electronic Computer Technique

Medical research is enlisting the aid of electronic computer techniques to help fight the crippling effects of Parkinson's disease or "shaking palsy."

The puzzling illness was first described by Dr. James Parkinson, a British physician, almost 150 years ago. Today, it is estimated that up to 500,000 people in the United States are suffering from the malady, which strikes additional thousands each year.

Researchers at the neurophysiology laboratory at the Veterans Administration Hospital in Minneapolis, Minn., have developed electronic equipment in order to measure the degree of disability, and to help diagnose and treat patients.

The project director, Dr. David D. Webster, assistant chief of neurology, says the hospital's testing program uses five methods of measuring muscle functions. Machines including a high-speed computer measure and plot changes in rigidity and tremor in the patient's limbs, their strength and flexibility, and patient's ability to react.

With this information, doctors can quickly and accurately detect any changes, however slight, in the course of the illness, the effects and the optimum dosages of various medications, and whether surgery might prove more beneficial in treatment.

Dr. Webster said that many machines have been built to measure tremor, "but almost nothing has been published showing consistent test results from day to day and week to week, and thus no statistical data is available on the effect of medicines or surgery."

Researchers at the VA hospital have developed a special machine to measure the work function of a limb, another device to test the patient's agility which prints results on a tape for comperative study, and a means to measure loss of muscle power.

Another test resulting in a computer score involves the ability of the patient to turn his wrist when told to twist a small doorknob-type handle back and forth as rapidly as possible.

"We have thus been able to isolate the inability to perform rapid alternating movements from rigidity, tremor and weakness, and we have found drug and surgical effects can help to change this situation."

Dr. Edward Mandell, director of the VA hospital, said the neurophysiology laboratory is presently engaged in measuring all of the pre- and post-operative Parkinson surgery done at the University of Minnesota. He said researchers are also following several hundred Parkinson patients in a long term study of the disease, including the effects of different medications.

"Deep brain surgery has been found to benefit more than 80 per cent of those operated on, but the degree of improvement is exceedingly variable," he said. "The work done by Dr. Webster and the research staff at the hospital will help to a large degree to identify those characteristics which will prove most amenable to surgery."

Crop Insecticide Hazard Termed Negligible

A chemical insecticide used to spray crops has only a negligible effect on persons living nearby, a study showed recently.

The study, made in the Phoenix area, compared city dwellers unexposed to insecticides with persons living less than 500 yards from sprayed fields who frequently complained about the insecticide, primarily because of the odor and nasal irritation, according to a report in the current *Journal of the American Medical Association*. Most of the exposed group lived within 50 yards of the sprayed fields and probably had as much exposure as any individuals not occupationally involved with insecticides, it was pointed out.

Results of the study "support the conclusions of others that hazards of insecticidal poisoning to persons with environmental or incidental exposure are negligible, " Robert S. Ganelin, M.D., Phoenix, Cipriano Cueto Jr., M.S., Atlanta, and G. Allen Mail, M.S., Tucson, concluded.

Agricultural insecticides are used in the Phoenix area most of the year with the heaviest applications to the cotton crop in July, August and September, the researchers explained. Parathion, an organic phosphorus insecticide, is used almost exclusively in the study area, and is generally applied by planes.

Nearby homes were frequently enveloped by drifting insecticide following applications, according to the report.

The high toxicity of some organic phosphorus insecticides is well known but proper precautions can eliminate danger to persons who work with them, the researchers said. With increasing use of these chemicals, they said, there has been growing concern about the possible hazard among unprotected persons, particularly in residential areas adjacent to treated crops.

A total of 122 volunteers were studied in an effort to determine absorption of the chemical, symptoms associated with insecticide poisoning, and laboratory evidence of chemical intoxication.

For comparison, the volunteers were divided into exposed, unexposed, and occupationally exposed groups and further subdivided into asthmatics and nonasthmatics. They were checked monthly from May through December, 1958.

Although the number complaining of symptoms was higher for the exposed groups, the differences were not significant for any month, it was found. Neither was there found a single individual with symptoms resembling those of organic phosphorus poisoning.

The differences in absorption between the city dwellers and those living near the treated fields were "small and not significant." Only one person, a farmer, produced laboratory evidenec of intoxication and he had no symptoms of poisoning.

Evaluation of the effect of insecticide on asthma is much more difficult than evaluation of its effect as a poison, the authors pointed out.

Many of the exposed asthmatics maintained that their asthmatic attacks were related to insecticide exposure. The authors said the complexity and variability of the disease made it impossible to draw definitive conclusions but, if insecticides do affect pre-existing bronchial asthma, their findings, indicate that the effect is a relatively minor one.

Flammable Fabrics

Don't set fire to your clothing. You might get burned.

Foolish and unnecessary admonition? Sounds that way. And yet, each year thousands of people are severely burned, some fatally, when their clothing catches fire.

If little girls wore trousers instead of skirts, the safety record would be better. Flimsy, flaring skirts of light, readily inflammable material, are easily ignited by brushing across a space heater or backyard grill.

Older folks often fall asleep sitting in a chair while smoking. The cigarette drops into the lap and—poof!

Small boys are often fascinated by matches or mechanical lighters. They will even hide in the clothes closet to strike matches, if they can get hold of a packet.

The problem of the fire hazards of fabrics is so widespread and serious that it received consideration by the House of Delegates of the American Medical Association at a recent meeting. The AMA leaders agreed that an education program to create public awareness of fire hazards of clothing is needed.

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ANTICOAGULATION AND FIBRINOLYSIS: NATHAN H. FRIEDMAN, M.D., GUEST EDITOR

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VIRCHOW AND CELLULAR PATHOLOGY (see page 629)

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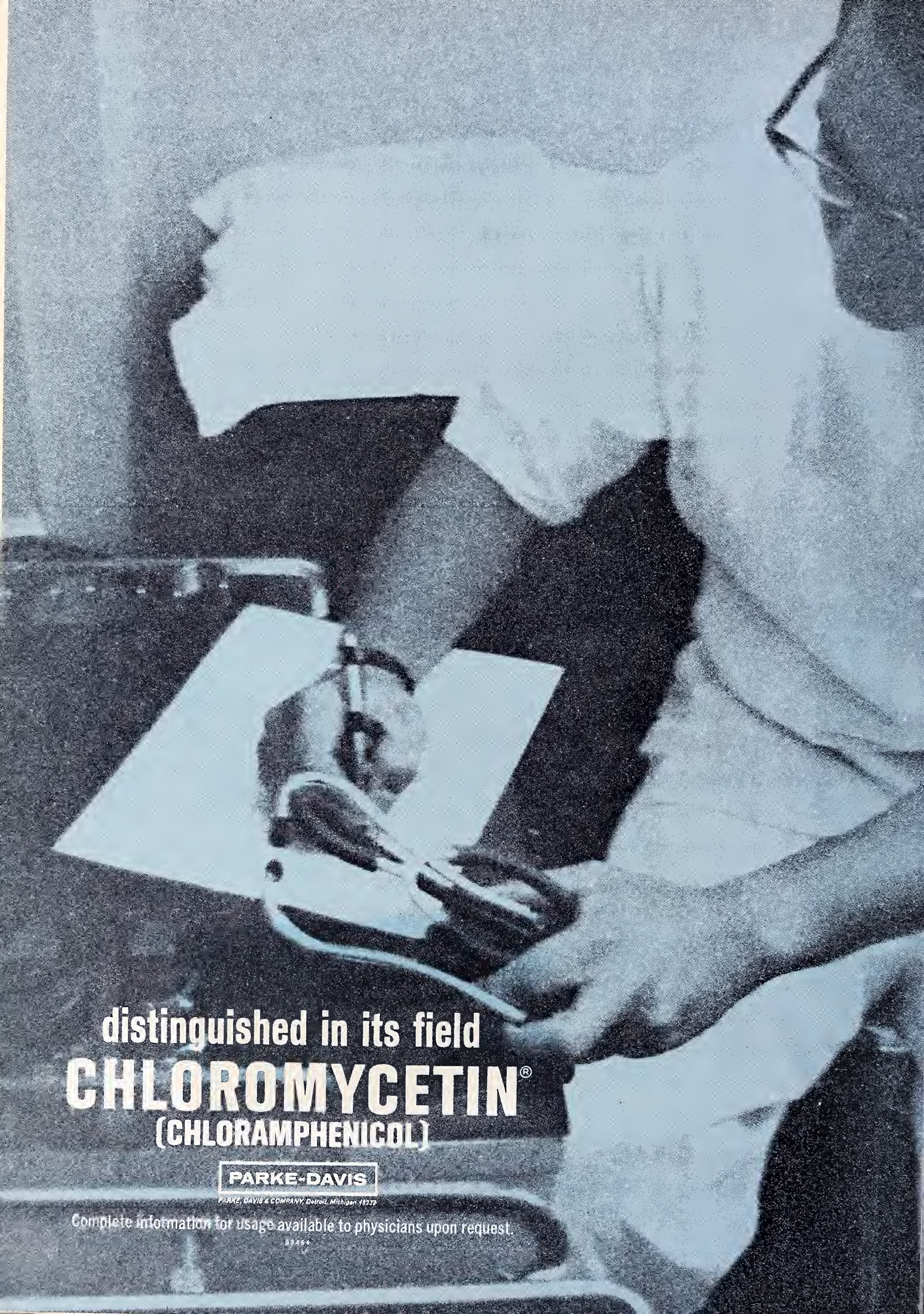

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Connecticut Medicine

editorials

Autoregulation And Collateral Circulation

The arterioles and small arteries are supplied with strong muscular coats that are capable of changing the vessel diameter at least 4 to 6 times and this makes them highly suited to the important role they play in regulating blood flow to individual tissues of the body. If blood flow to a leg or an arm is stopped for as long as one minute and then reinstituted the flow immediately increases 2 to 6 times more than it had originally been. This rapid flow continues until the metabolic deficit caused by the lack of flow is made up. This phenomenon is termed Reactive Hyperemia. It is a local autoregulation of blood flow and is one of the most powerful of all factors that control blood flow in most of the tissues of the body including especially the muscles, heart, brain and kidneys.[1]

The blood flow to the limb need not be stopped to give rise to local autoregulation. Decreasing it to one-half of normal, immediately institutes the mechanism and within approximately one minute the flow will have returned to near its normal value. Such an experiment illustrates that ischemia automatically promotes vasodilatation of arterioles resulting in return of almost normal flow. This type of autoregulation is not a nervous reflex phenomenon for it occurs even when the nerves are destroyed. Thus the tissues have their own intrinsic mechanism for "protecting" their blood flow. If any extraneous factor were to decrease the flow, the vessels respond to the local ischemia by dilating, thereby almost correcting the deficit in flow.

On the otherhand if an extraneous factor causes excess of flow to tissues the opposite occurs: the vessels automatically constrict and in this way divert the cardiac output for use elsewhere in the body. In short the local autoregulation mechanism operates in response to the requirements of tissues varying the blood flow in proportion to needs. The precise mechanism for autoregulation has yet to be determined but it is known that reduction of oxygen itself can cause it. It is also believed that ischemic tissues release a vasodilator substance, a polypeptide such as bradykinin. The importance of local autoregulation, of course, to insure a continual supply of adequate nutrition to the tissues both normally and during excessive activity.

Blood flow through the coronary system is regulated almost entirely by a local mechanism in the heart in response to the needs of the cardiac musculature for nutrition, whether the nerves to the heart are intact or severed. Whenever the vigor of contraction is increased regardless of cause, the rate of coronary blood flow simultaneously increases. Conversely decreased activity is accompanied by decreased coronary flow. During ventricular systole blood flow through the left ventricle is greatly reduced thereby accumulating vasodilator metabolites. The resulting oxygen lack is followed by vasodilatation during diastole. In this way by autoregulation the heart regulates blood flow to the cardiac musculature in proportion to the metabolic need for oxygen by the muscle fiber.

It is immediately obvious that this local autoregulation is almost identical with that which occurs in skeletal muscles of the body. Both in skeletal muscle and heart a decline in blood flow caused by arterial disease tends to render these tissues hypoxic. If the decline in circulation is slow, the hypoxia may be expected to lead to local vasodilatation. It

THE COVER

VIRCHOW AND CELLULAR PATHOLOGY

JUST past his thirty-fourth year, in 1855, Dr. Rudolf Virchow (1821-1902) while professor at Würzburg University, Germany, propounded his theory of cellular pathology. Lecturing and demonstrating at his specially made desk in the Würzburg Krankenhaus, the slight, short, fiery professor used microscopes to convince students that cells reproduced from other cells, and taught that disease results from disturbance of cells by injury or irritants. Later, in Berlin, Virchow continued to lead international medical thought, and to teach, to engage in research, to write, to edit, to explore new fields, and to serve his community politically, until his death.

is probable that this is a potent mechanism for producing a collateral circulation. These facts offer a good physiologic reason for patients who suffer from arterial disease in limbs or heart to engage in some form of physical activity as the best way to promote a collateral circulation. If the arterial pressure were to decline temporarily as in a faint or in shock, then autoregulation will insure adequate nutrition to heart and brain, by dilatation of the small arteries and arterioles.

Autoregulation is probably the basic mechanism for regulating cerebral blood flow. In the normal individual 15 per cent of the cardiac output flows through the brain or 750 M.L. per minute. This is regulated principally by concentration of CO_2 and O_2 in the cerebral blood. Either excess of CO_2 or diminished O_2 causes marked vasodilatation. Anytime that the cerebral blood flow declines, whether it is due to drop in arterial pressure or developing cerebral arterial disease, CO_2 will build up, O_2 will decline in the cerebral blood and blood flow automatically increases thereby correcting these two conditions. For this reason cerebral blood flow remains constant within limits of 60 to 180 mm.Hg. Here again one finds a very important local autoregulatory mechanism for maintenance of blood flow to the brain in proportion to its metabolism, a mechanism which like in the limbs or heart tends to promote collateral circulation in patients suffering from cerebral arterial insufficiency.

There are other functions in tissues besides nutrition. For example, blood flow through the skin is to a great extent controlled for the purpose of eliminating or conserving body heat. In the kidney, blood flow is mostly not for the supply of nutriments to the renal tissue but instead for the control of urinary output. In the skin blood flow is controlled entirely through nerves. In the kidney, however, except during shock and exercise blood flow is under the control of local factors.

Over a wide range of blood pressure 80-180 mm. Hg. the blood flow through the kidney is not dependent upon the arterial pressure level. During this range there is self regulation of blood flow by the kidney itself. It does not depend on the central nervous system because the same phenomenon is found in transplanted kidneys. Since the regulation is not dependent upon nutritive requirements of the kidney, the explanation for the phenomenon does not rest upon the mechanism of oxygen lack and increase in metabolites. The true explanation is not yet at hand but several ideas have been advanced. One by Homer Smith states that as blood pressure goes up afferent arterioles constrict, but if blood pressure goes down efferent arterioles dilate allowing more blood through. Pappenhemier explains autoregulation by the kidney by another mechanism: as the blood goes through the kidney vasculature, plasma is skimmed off and red cells go on; the hematocrit rises and when it becomes 50 or more then viscosity interferes with flow; the net results of increase in blood pressure is thus to raise the resistance in distant glomeruli. There are other theories, but up to the present time, autoregulation in the kidney is a fact although its explanation is still to be settled by further study.

The fact that autoregulation exists in the kidney should not obscure the fact that its afferent and efferent arterioles have well developed smooth muscle walls which are highly innervated by sympathetic nerves. Strong stimulation of the sympathetic nerves diminshes blood flow through the kidneys almost to O. In the normal resting person the degree of sympathetic activity upon the renal vessels is ordinarly insignificant. On the otherhand when excessive blood flow is needed elsewhere as in muscles during severe exercise or in stages of shock, sympathetic stimulation can greatly reduce renal blood flow allowing blood to be diverted into areas requiring increased flow. This mechanism can be of great value to the temporary function of the body and does not seriously reduce the effectiveness of the kidneys which can go on for hours without renal function and not suffer serious consequences.

From what has been said above it is clear that autoregulation is an important mechanism by means of which organs regulate their own blood supply under a wide range of activity. It is a mechanism of great importance in overcoming the disastrous effects of arterial disease in muscles, heart and brain. We must strive to utilize this mechanism in our patients.

L.H.N.

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Prognosis In Myocardial Infarction

Until recently there has been uncertainty and a rather pessimistic outlook for patients with myocardial infarction. Such uncertainty, understandably, was discouraging for many patients, so much so, that they were often unable to utilize what might otherwise have proved to be many useful and enjoyable years. From the patients standpoint, then, once he has recovered from his acute attack, a most important aspect is what lies ahead of him. This involves not only good medical supervision, in which we are now quite expert, but matters of prognosis. Answers to this question come from clinical experience and epidemiologic observation. Such knowledge could prove of great practical value

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to the physician and great moral support to the patient. It could help to allay life-long anguish formerly imposed on victims of myocardial infarction and augment the extent of rehabilitation to a useful and productive life in such patients. Improvement in outlook has come about because of improved diagnosis and therapy and because of a better understanding of the natural history of this disorder.

The question of prognosis of course cannot be confidently approached until the completed course of the disease has been observed in a large number of patients. When the diagnosis of acute myocardial infarction first became clinically feasible the prognostic outlook for both acute attack and long term survival was considered poor. In part this was due to the fact that the most serious patients were taken to a hospital and such series comprised but a small part of the number of similar though less sick patients in the total population and the many who were not even diagnosed because of mild or atypical symptoms.

A recent paper by Pell and D'Alonzo[1] has undertaken to answer several questions about immediate and long term prognosis in myocardial infarction based upon a study of 1331 male patients, employees of DuPont Co. who were stricken with myocardial infarction. Then data was analyzed to answer questions which all physicians are called upon to do. One question: What are the chances of surviving an acute attack is answered by what seems to be sobering statistics. 336 or 25.2% died in the first 24 hours and 399 or 30% died within the first month. This is consistent with the findings in the Framingham study[2] in which a fatality rate of 38.7% was encountered in the first three weeks after onset of an initial acute coronary attack was noted. These figures are higher than the DuPont ones because they involve general population rather than the selected group of individuals admitted to the hospital. However, although the three week fatality rate in the total population in the Framingham study was 38.7, in the patients in the same community sick long enough to be hospitalized it was only 22%, not much different than in the DuPont study. It is obvious that the prognosis in acute coronary heart disease, seems poorer than it has generally been assumed to be. These figures are in sharp contrast to those involving so-called "good risk" cases in which recognizable acute myocardial infarction was present, only 1.8% of the patients surviving the first 48 hours died.[3]

Such experiences have important therapeutic implications in acute coronary attacks. They suggest that early recognition, prompt admission to a hospital with constant supervision even to the extent of continuous monitoring for the first 48 hours can be of crucial importance, whereas it appears one may relax ones efforts somewhat, thereafter, at least in patients with mild to moderate attacks. Of those that survived one month, the one year survival rate was 90.5%. Of those under 35 only one death is recorded. Between 30-45 25% of deaths. Between 60-64 37.2% of deaths. The immediate prognosis seemed to be determined by the existence of hypertension in whom the immediate mortality was 43% in 55-64 age group, whereas in the normotensive it was 29.5%. Another factor in immediate prognosis was the presence of serious pre-existing heart disease as evidenced by bundle branch block especially of the left type in which the immediate mortality was 57.1%.

One very important point the authors bring out and which has medico-legal implications is that those individuals who had their attacks during the day time and at work had an immediate mortality of 21.8%, wheras those whose attack occurred during the night had a much poorer prognosis exhibiting a mortality of 38.4%. Can it be that the defense mechanisms are poorer at night than in the day time? Does moderate or even strenuous physical activity protect against severity of the attack? Is there a diurnal variation in ventricular excitability or vulnerability, so that fatal arrhythmias are more common at night or is it simply that, as Pell and D'Alonzo claim, that during the day there is greater accessibility to immediate medical attention? Whatever the explanation, the degree of physical activity at the time of the attack, appeared to have little if any effect on the immediate prognosis.

If a person has weathered the first 30 days after an acute infarction then the 5 year survival rate is somewhat better than has been previously thought. There were 74% of 932 patients alive or 77% of the total. The expected survival rate without infarction is 95.8%. Age seemed one factor to be involved since 81% of those under 45 years of age survived as compared to 72% in older age groups. Hypertension was another factor adversely affecting 5 year survival since 66% survived as compared to 81% among the normotensives. Overweight played only a slight role in reducing survival while socio-economic status showed no effect in survival rate.

It is clear that the outlook for victims of myocardial infarction is steadily improving. In 1941 Bland and White[4] reported a 5 year survival of 49% of 162 patients with myocardial infarction in those who survived the first 30 days. In 1954 Cole, Sinjian and Katz reported a 5 year survival of 66.7% in those who survived the first 2 months and now Pell and D'Alonzo report a survival rate of 77%. We would like to hope that such improvement in survival is the result of early diagnosis, quick adequate therapy and good post-infarction supervision.[5] Now with improved prognosis as a justification of our efforts, we are in possession of knowledge that should help a person to know what is ahead for him thereby adding not only years to life but useful and happy life to years.

L.H.N.

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Fibrinolysis By Drugs

There is now good evidence of an active fibrinolytic mechanism in the blood. Under certain conditions it becomes overactive leading to hemorrhagic states.[1] Under other circumstances, the fibrinolytic mechanism is inadequate and then thrombotic states occur. Under normal circumstances it is no longer speculative to ascribe to it the function of removing fibrin deposits from blood vessels and to lyse the fibrin which contributes the major part to most occlusive thrombi. Whether or not we accept the concept of a dynamic equilibrium between coagulation and fibrinolysis there must be times when fibrin is deposited in vascular channels and must also be removed if occlusion of the vessel is not to take place.

The wide range of the contributions to the second fibrinolysis "Workshop"[2] indicates that the fibrinolytic system as it should now be called, plays a part in a number of processes, not the least of which is inflammation and many intravascular functions. Fibrinolysis undoubtedly has considerable relevance to occlusive vascular disease, where it has failed, and it is time for us to consider how it may be harnessed for treatment.

Tsapagos[3] has lately discussed two ways for utilizing our knowledge of fibrinolysis in therapy, one he termed enzymatic and the other pharmacologic. Enzymatic fibrinolysis about which rather more is known, is directed towards the treatment of established thrombotic occlusion. It consists of increasing fibrinolytic activity by the injection of such exogenous activators of plasminogen as streptokinase. The treatment may be given systemically or into the affected blood vessels. There is now overwhelming evidence that it is possible to lyse an occlusive thrombus and restore the patency of the vessel in this way.[4]

There are, however, factors which limit the successful use of "thrombolytic" therapy. One is the site and (because local treatment may be preferable), the accessibility of the thrombus, and one is the time at which attempt at lysis is undertaken. Cerebral tissue is severely damaged within a few minutes of being deprived of its blood supply so that by the time therapy is undertaken, only marginal, if any, benefit can be expected. The heart muscle survives longer but rarely long enough to expect revitalization of the infarcted area from re-establishment of the circulation by thrombolysis.

Heroic efforts have been made to administer thrombolytic agents into an occluded coronary artery.[5] However, unless the treatment would be of unusual benefit most people would be deterred by the difficulty of systemic administration, let alone those of cannulation of the coronary sinus. Even the experience of Dewar *et al*,[6] using the intravenous route, has been discouraging. Of course, in arterial thrombosis of a limb, the situation is different because there is more time. Tsapagos by streptokinase, and Nahum, Kline and Fishbein by plasmin mixtures were able to lyse thrombi in both arteries and veins. Tsapagos's experience in eight patients was less encouraging than those of Nahum *et al* in experimental thrombosis. He obtained partial dissolution in five and only in three was arterial patency fully restored. This may have been due to the extent of the pathologic occlusion rather than enzymatic failure but certainly enzymatic fibrinolysis alone without surgery was mostly inadequate.

The pharmacologic approach to fibrinolysis aims at enhancing the natural fibrinolytic activity of the blood over long periods, the intention being therapeutic as well as prophylactic, the latter of which is analogous to anticoagulant therapy. In fact if effort is made to dissolve an intravascular thrombus and it is successful it leaves a denuded endothelial surface where the clot was, over which clotting would take place again unless it were prevented by anticoagulation or a fibrinolytic agent. Therefore all efforts at thrombolytic therapy must be followed by prophylactic therapy at least until the denuded endothelium has healed over.

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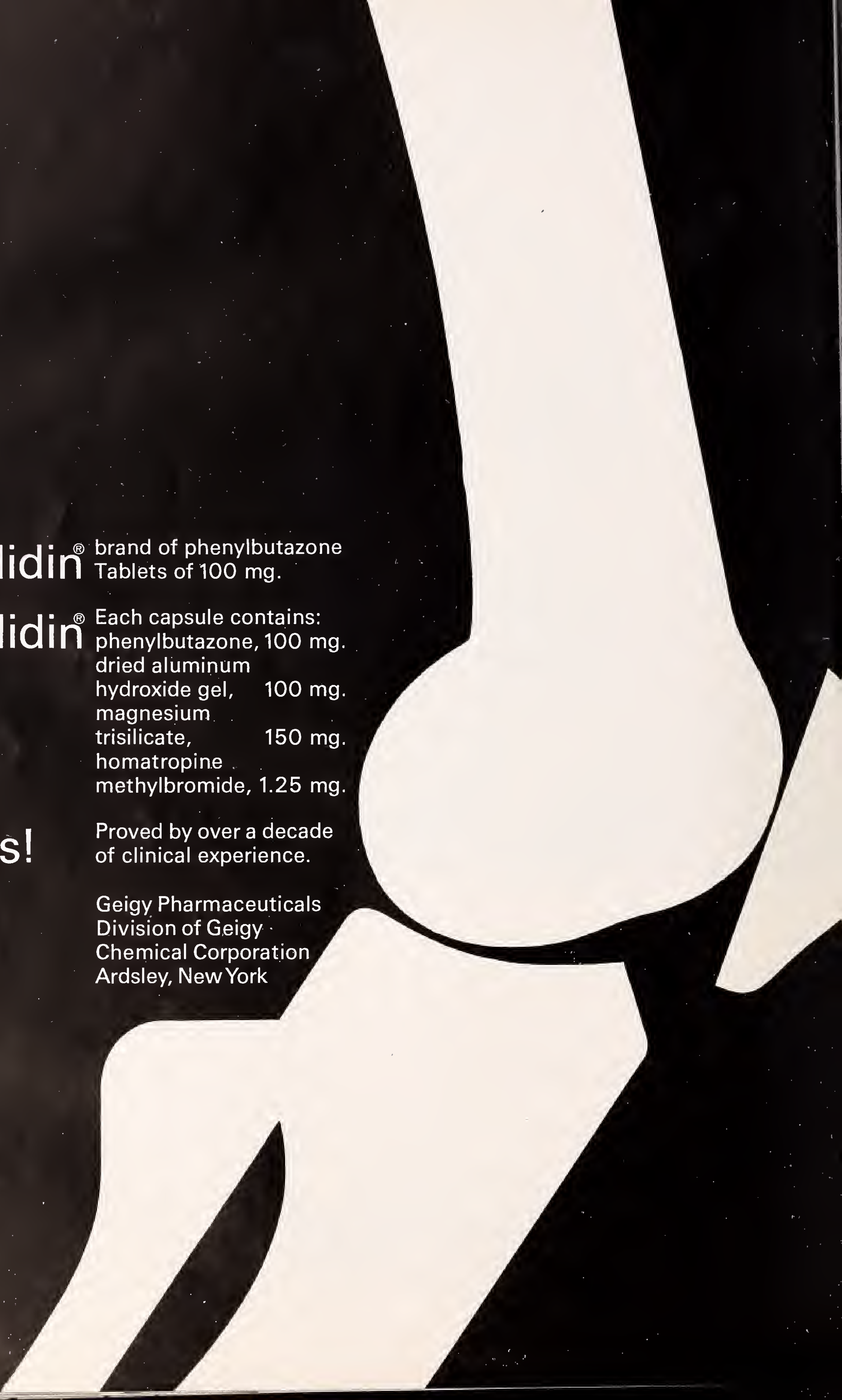

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There is evidence that endogenous fibrinolytic activity is lower in patients with arterial disease than in healthy people of the same age.[7] Furthermore Naimi *et al*[8] have reported that fibrinolytic activity is lower in the arterial than in the venous blood of patients with coronary artery disease, this difference being greater than in healthy people. It is clear from this why patients with atherosclerosis are more susceptible to thrombosis and why such patients require antithrombotic vigilance preferably by agents that can prevent thrombosis.

In the proceedings of the Workshop, Fearnley and Chakrabart[9] summarize their experience with a number of drugs which they have found to enhance the spontaneous fibrinolytic activity of blood in patients with arterial disease studied daily in the fasting resting state. Of 50 patients with various forms of occlusive vascular disease, 60 per cent were considered to have low blood fibrinolytic activity as judged by venous clot lysis times repeatedly greater than 7 hours. They found that sulphonurea drugs, tolbutamide and chlorpropamide, will produce a considerable elevation of fibrinolytic activity when given daily. However, they cannot be used indefinitely because resistance develops in many patients after several weeks of treatment.[10]

Testosterone and nandrolone[11] when given by injections in large daily doses seem to produce a sustained fibrinolytic effect. These anabolic steroids when given by mouth have proved disappointing, however, since resistance developed in most patients similar to that found when the sulphonureas were employed. More promising results have been obtained by these authors with phenformin, which appears to raise the fibrinolytic activity of the blood without inducing resistance, judging from patients readmitted for study 3 months after starting treatment. Here, however, there is also a drawback since the dosage is limited by gastric intolerance.

Very interesting in this respect are the corticosteroids and corticotrophins[12] which increase fibrinolysis in patients with both inflammatory and non-inflammatory conditions. The effect seems to be sustained and although these drugs may not be suitable for the treatment of occlusive vascular disease, this hitherto unknown fibrinolytic action may be relevant to their known anti-inflammatory effects.

One drug that has recently come into use in treatment of occlusive vascular disease is phenylbutazone.[13] It has been known for a long time that this drug has anti-inflammatory properties and it has been widely recommended in thrombophlebitis as well as acute arthritis. It has now been tried on 57 patients with acute myocardial infarction in doses of 400 mg. daily for the first 4 days. The impression is growing that in the majority of patients the extent of necrosis is reduced, the hospital stay is shortened and convalescence is also shortened. Preliminary observations on fibrinolysis suggests this drug can enhance fibrinolytic activity.

The multiplicity of drugs which have been found to enhance endogenous fibrinolysis suggests that others may exist or may be fashioned that are free of disadvantages. Fearnley and Chakrabarti noted the healing of incipient gangrene in a number of patients treated with phenformin or testosterone, an observation which could be tested by treating a larger number of patients.

The long term effects of increasing fibrinolysis by drugs in arteriopathy still remains to be investigated. It is an undertaking fully as important as the extensive studies on the use of anticoagulants. It might turn out to be more important since anticoagulants are not without danger and do not lyse clots once they have formed, whereas fibrinolytic drugs can lyse clots and restore the integrity of the blood supply to a vital, but obstructed region. Fibrinolytic drugs certainly offer a new approach to a clinical problem at present beset by therapeutic difficulties.

L.H.N.

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Rationale Of Thrombolytic Therapy In Arterial Occlusive Disease

Based upon what we know, whenever an intravascular clot remains undissolved, it is probably due at least in part to an insufficient amount of plasminogen activator in the blood. It is this fact which has led investigators in this field to search for enzymes and drugs that will overcome this deficiency in thrombotic states. One method has been to administer the final enzyme plasmin[1] which acts directly to cause dissolution of fibrin clots. Other methods have depended on production of activator with streptokinase or actual use of activator like urokinase. Another method as noted above is the use of fibrinolytic drugs.

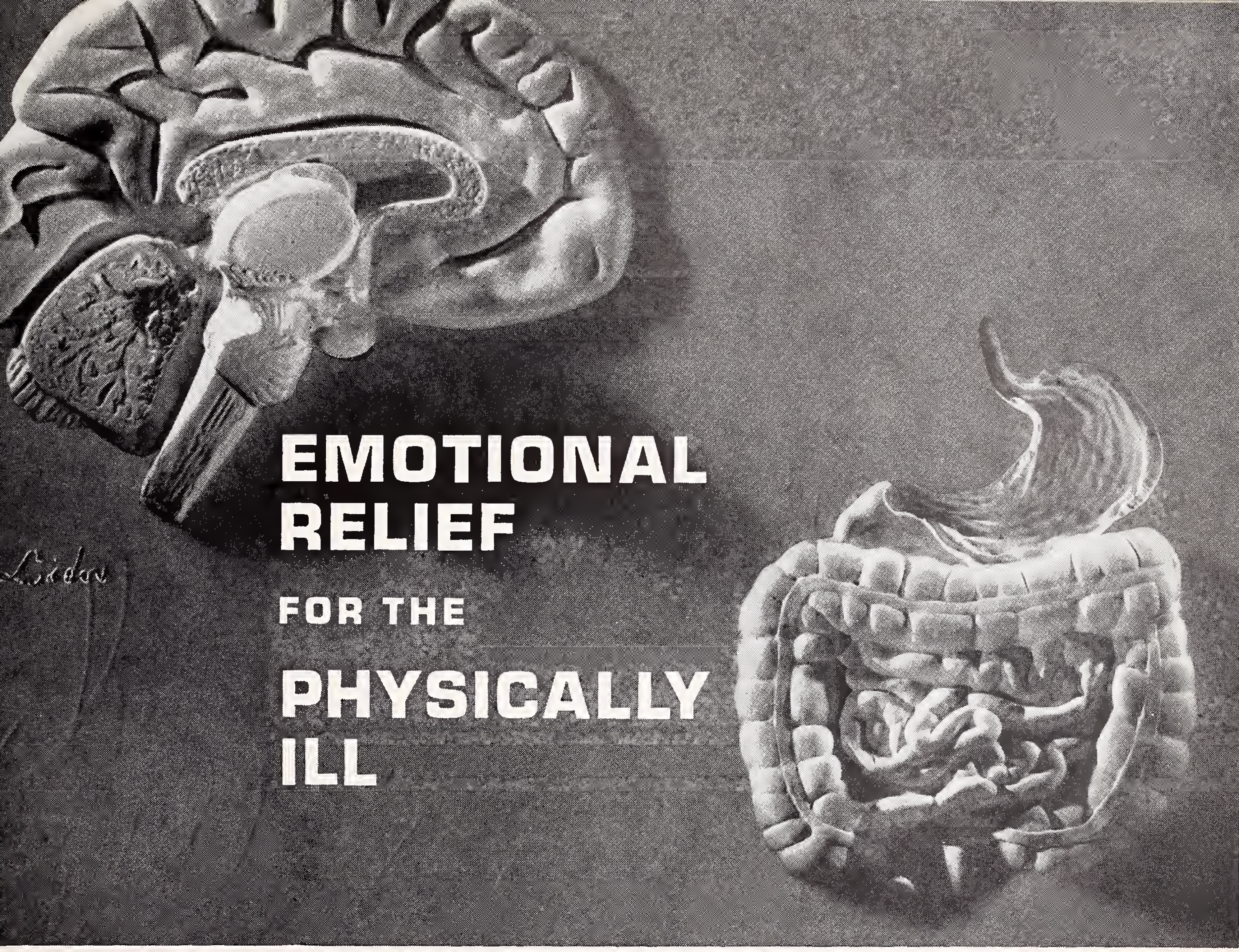
The type of patient that would properly be suitable for fibrinolytic therapy has received some attention in several symposia on this subject.[2] Elderly and debilitated patients with venous thrombosis and central vein thrombosis of the retina were considered suitable. On the other hand patients with arteriosclerotic disease in which a thrombus is the final epside in either the coronary or cerebral arteries were considered questionable or unsuitable. Without doubt the opinions on this subject were colored by the dangers inherent in the enzymatic therapy as it is presently available rather than a theoretical consideration of the possible advantages of thrombolysis in thrombotic arterial disease if methods to dissolve the clot were not hazardous and clot dissolution were easy to achieve. We are in a stage of rapid advance in the fashioning of drugs that will be fibrinolytic and therefore we must try to answer the question whether there is a rationale for thrombolysis in arterial disease, given a safe and dependable agent.

One of the difficulties that the clinician faces when he is confronted with the necessity of making a decision on employing fibrinolytic agents in arterial occlusive disease, is the absence of a precise test of thrombosis in an inapparent site. When for example, a coronary occlusion or a cerebral occlusion takes place we do not precisely know whether the occlusion is caused by a thrombus, or by a subintimal hemorrhage, or the rupture of an atheromatous abscess or merely by progressive atherosclerotic narrowing. It is probable that no more than one half of all cases of coronary occlusion are caused by a thrombus. If we had a laboratory test for thrombosis at an inapparent site it would, of course, reduce the number of patients in whom we could expect any benefit from thrombolytic therapy. But there would still remain the question whether even in thrombosis such therapy would be beneficial.

Cerebral tissue is severely damaged within 2-4 minutes of being deprived of the blood supply so that by the time therapy is undertaken only marginal, if any, benefit can be expected. The heart muscle survives much longer, but rarely long enough to expect revitalization of the infarcted area. Of course in arterial thrombosis of a limb the situation is different because there is more time, but the question still remains what benefit can be expected from producing thrombolysis in arterial disease when therapy is undertaken after an irreversible lesion has already taken place.

There are several physiological considerations which make it mandatory to attempt to restore the continuity of an artery whose obstruction led to an infarction. One is the well known fact that almost every infarct is surrounded by a zone of compromised cells in the peri-infarcted area. This region suffers from a compromised blood supply which is not sufficient to maintain normal function, yet adequate to maintain viability. The size of this peri-infarcted area, of course, must vary, but if the circulation could be restored to it, the infarct will be much smaller and will be limited to the first necrotic zone. Ordinarily the peri-infarcted area is kept alive by blood received from collateral channels. Some of which close by further thromboses because of reduced velocity of blood flow through them. There is therefore danger that the peri-infarcted zone may also go on to necrosis thereby enlarging the amount of damage. By opening the plugged artery early we may expect to restore the nutritional integrity of the peri-infarcted area, and reduce significantly the size of the infarct. A good blood supply to the peri-infarcted zone should also accelerate the healing process and significantly reduce the time necessary for healing of the infarct. A recent experiment by Nydick on the use of thrombolytic therapy in experimental canine coronary occlusion, while not comparable to the natural situation occurring in man, supports this explanation.

Another important reason for re-establishing the continuity of a plugged artery is that this will help to avoid blood diversion from other areas of the heart to the compromised region. We must remember that if viability persists in a peri-infarcted zone, it is due only to blood reaching it from other regions. Such an occurrence could lead to reduced blood supply to an area from which the blood diversion has taken place. In saving the life of one area, other regions, by yielding part of their blood supply could also suffer.[4] The extent of impairment that might occur under such a situation has never been studied in the heart. It has, however, been studied in the brain by Reivich *et al*[3] who showed how blood from the basilar system can be diverted



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through the vertebral into the axillary artery when the subclavian on this side is partially or totally occluded. The blood diversion away from the brain can be sufficient to produce serious symptoms of cerebral anoxia. It could and probably does do the same in the heart under similar stressful circumstances.

It is apparent that if we could restore the continuity of a plugged artery by thrombolytic therapy, then the original size of the infarct would not be enlarged by further necrosis in the peri-infarcted zone. The peri-infarcted zone would quickly recover its viability and contractile power. The regions of the heart that would be called upon to share their blood supply with the peri-infarcted zone, would retain their blood supply and not suffer from hypoxia. These are good reasons for thrombolytic therapy in arterial occlusion and a series of patients so treated, should show a more benign course, more rapid rehabilitation, less damaged hearts, and a lower mortality. Preliminary studies on a small series of patients supports this expectation.[5]

One difficulty in a statistical approach to obtaining data on the value of such therapy at the present time, is that we have no way of isolating the thrombotic from the non-thrombotic occlusions and until a good laboratory test for a thrombus at an inapparent site becomes available, the statistics will be difficult to evaluate. However, if anti-thrombotic therapy by drugs can be perfected, it would be a method not difficult to administer, not frought with serious complications and therefore worthy of trial in all cases especially of coronary occlusion.

L.H.N.

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Epsilon-aminocaproic Acid (EACA)

The fibrinolytic system existing in blood consists of a protein, plasminogen which when acted upon by an activator obtained from tissues is converted into plasmin which then breaks up the fibrin in clots. Ordinarily every thrombus formed contains in addition to fibrin also plasminogen which when converted into plasmin by a circulating activator promptly produces lysis of the clot. Much morbidity and mortality is the result of intravascular clotting and much investigative effort has been directed to produce an effective thrombolytic agent.

The opposite of thrombosis can also occur though less frequently. Nevertheless hemorrhagic states do occasionally pose a serious problem in control of bleeding. It is well known that elevated fibrinolytic activity in vivo is a major contributing factor in severe hemorrhage observed in a variety of disease states. Parallel to the search for a safe fibrinolytic agent in thrombosis has been the search for an antifibrinolytic agent for use in hemorrhagic states.

In 1953 after a long period of screening for compounds that have antiplasmin activity it was discovered, that epsilon-aminocaproic acid (EACA) at concentrations as low as 10^{-5} molar possesses antiplasmin activity and therefore could neutralize the fibrinolytic effects of plasmin. This substance EACA apparently not only has antiplasmin activity but can also act by inhibiting plasminogen activator at concentrations much lower than those necessary to produce plasmin inhibition. Regardless of the exact site of action it is agreed that EACA is a potent inhibitor of fibrinolysis in vitro.

The urine normally contains an activator of plasminogen called Urokinase which could lead to impairment of hemostasis by promoting lysis of fibrinous clots in the urinary tract. Looked at in one way this mechanism is a protective device to prevent plugging of the urinary tract when bleeding into it occurs. At the same time bleeding in the urinary tract can assume alarming proportions after prostatic resection, in carcinoma of the prostate, during anticoagulation therapy and thrombocytopenic purpura. Especially in elderly patients following even average prostatic resection, blood loss might have serious consequences. The average blood loss can be as high as 1800 m.l. although it may be as low as 200 m.l. Up to the present time all kinds of treatment from the use of local catheters to adrenosem, premarin and lipomul have not led to great reduction of bleeding. Thus either in hyperfibrinolytic states where one can bleed into tissues and body cavities or in bleeding from the urinary tract because of the urine containing urokinase, (a plasminogen activator) there is great need for a substance that could block the plasminogen-plasmin system and reduce the hazard of uncontrolled bleeding. It is therefore logical that if EACA prevents fibrinolysis in vitro, that it should be investigated for possible usefulness in the treatment of patients with hemorrhage due either to a hyperfibrinolytic state or to failure of clotting in the urinary tract.

EACA has been tested by McNichol *et al* who established the rationale for its use. After its use prostatectomy patients bled less in the first 24 hours than did untreated controls and this allowed for earlier removal of drainage tubes and reduced the period of hospitalization. The authors believed that the treatment caused a reduction in physiological levels of urokinase in the urine and thereby prevented lysis of fibrinous clots. Andersson and Nilsson confirmed McNichols results. They compared blood loss among 11 patients treated with EACA after prostatectomy, with 9 patients not so treated. The former lost 132 m.l. of blood compared with 449 not receiving EACA, thus confirming the value of EACA in the control of hematuria following prostatectomy.

EACA is rapidly absorbed following oral administration, reaches peak levels in 2 hours, has a high renal clearance and is rapidly excreted unmetabolized. It is easy to achieve a concentration required for inhibition of a systemic fibrinolytic state and because of the renal concentrating mechanisms, effective inhibitory levels in the urine can be maintained in the absence of systemic EACA action. But of course since the kidney is the primary source of excretion of the drug, the compound may accumulate in patients with decreased renal function, in whom much smaller doses would have to be used to prevent generalized intravascular thrombosis.

There are many conditions in which hyperfibrinogenemia occurs, from physiologic ones like severe exercise and anoxia, to post-operative ones, particularly in lung resection and open heart surgery, to obstetrical complications such as abruptio placenta, intra uterine retention of a dead fetus and amniotic fluid embolism. The condition also is found in some neoplastic diseases, leukemia, hepatic cirrhosis and many others even iatrogenically induced. All these are associated with hemorrhagic complications which in text-books are commonly reviewed under the heading of hypofibrinogenemia because low plasma fibrinogen levels are commonly observed as the end result of increased fibrinolysis.

Hemorrhage associated with hyperfibrinolysis frequently develops with great suddenness and is of extreme gravity requiring prompt and energetic treatment. In life threatening situations human fibrinogen infusions or fresh whole blood are emergency measures. However, the well proven therapeutic efficiency of fibrinogen must be weighed against the hazard of producing homologous serum jaundice, since the fibrinogen is obtained from upward of 1,000 or more donors in the preparation of a single lot. It is therefore not surprising that the reported incidence of serum hepatitis following fibrinogen infusion has ranged up to 35 per cent. Even so fibrinogen alone may not always be adequate therapy for hyperfibrinolysis. Ende has recently described such a patient in whom fibrinogen was of no value and in fact may have been made worse by it.

If we understand that during hyperfibrinolysis there is an increase in plasminogen activator in the blood, then we have the rationale for the use of EACA in such states, since EACA blocks not only the formation of plasmin from plasminogen but also blocks plasmin lysis of clots. Its use has now been reported in a variety of bleeding states: after open heart surgery, during chronic hepatitis, in hemophilia and in certain hematological disorders such as aplastic anemia, certain thrombocytopenic purpura cases, and in terminal leukemia, with very encouraging results. Oozing of blood associated with monocytic leukemia, hemorrhagic purpura with thrombocytopenia and uncoagulable blood, prostatic cancer complicated by hemorrhage all responses to I.V. EACA. Also the hyperfibrinolytic state induced by infusion of plasminogen-streptokinase mixtures in thrombosis, likewise responded to intravenous use of EACA.

Over 1,000 patients have thus far received EACA. Heart lesions have been described in one patient receiving it for bleeding due to metastatic prostatic carcinoma. Although intravascular clotting is possible, no unequivocal case has thus far been reported but such a possibility does exist and Dameshek in a panel discussion did describe a patient with lymphosarcoma and fibrinolysis who developed thrombotic manifestations after EACA. Obviously titration of administered dosage is important. Since thrombotic complications can occur, the usefulness of EACA in the treatment of hyperfibrinolytic hemorrhage and hematuria will be determined only after more exact knowledge of the safe and effective dose has been acquired. However, in life threatening hemorrhage associated with definite hyperfibrinolysis, we now have EACA which should be administered as part of the total treatment of the patient.

L.H.N.

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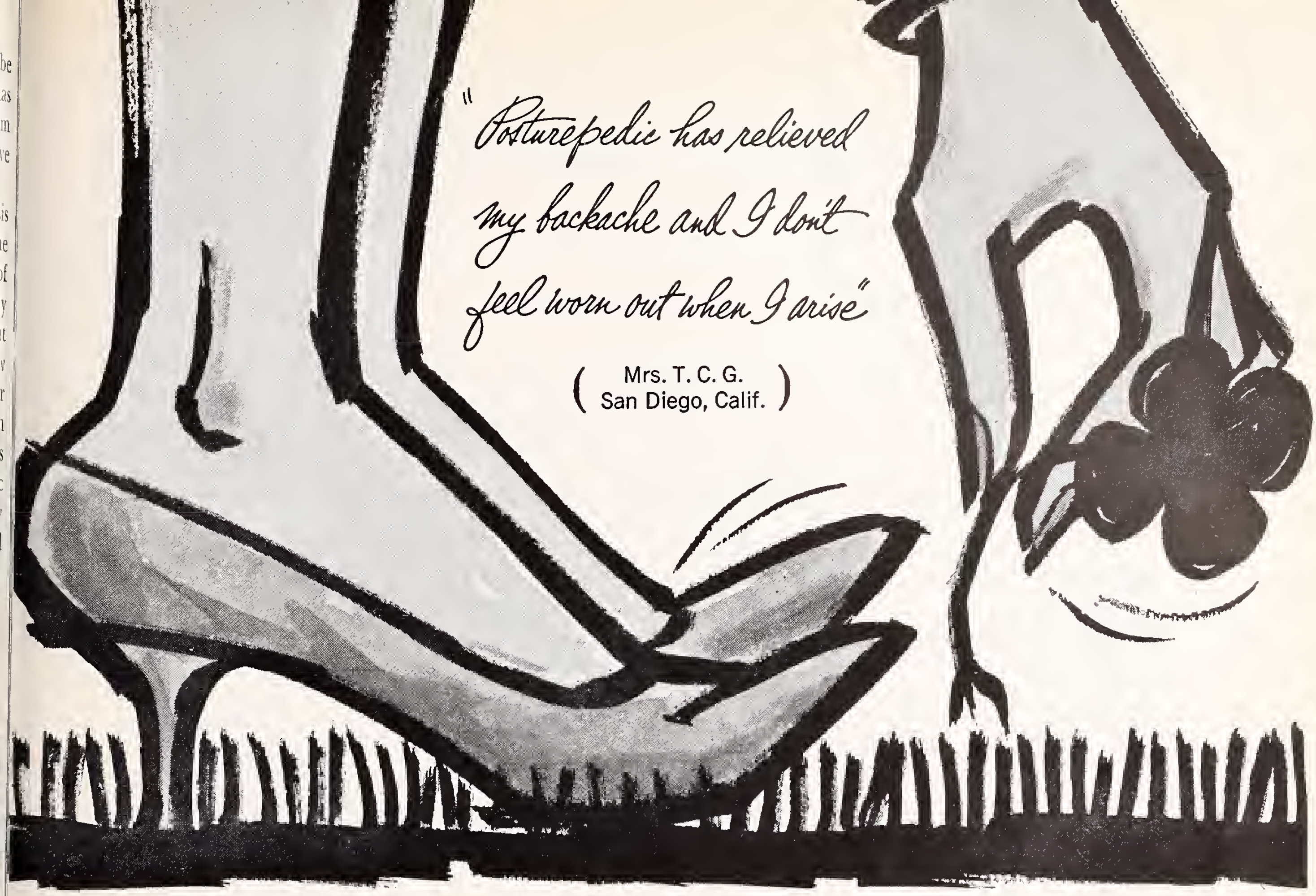
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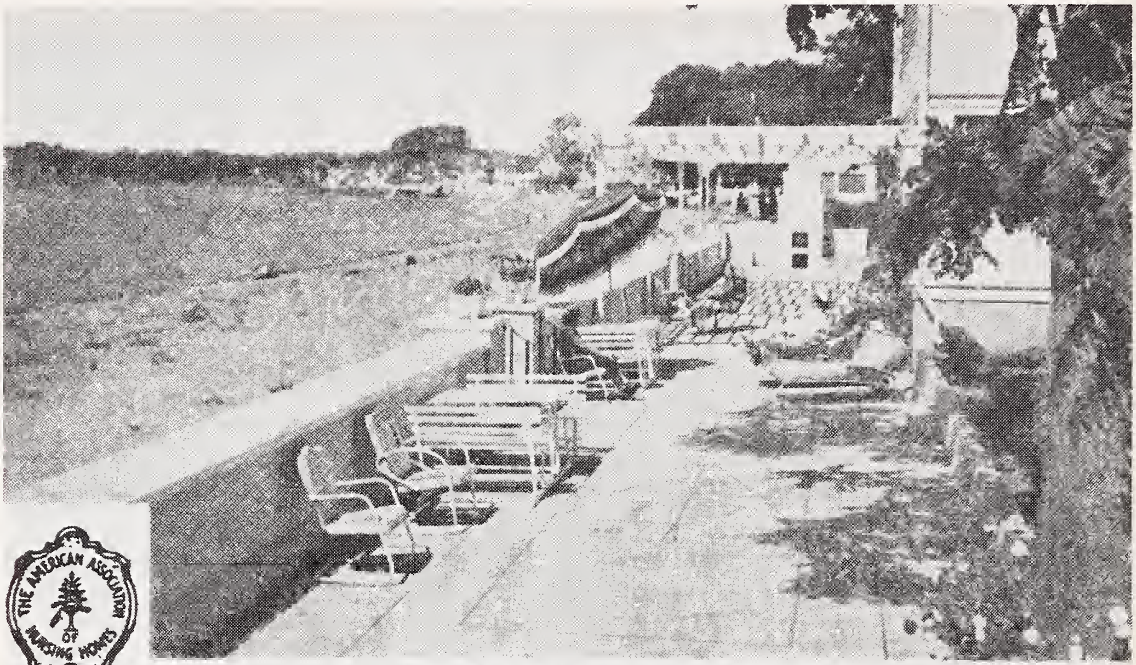

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Atherosclerosis And Thrombosis

The association between atherosclerosis and thrombosis is very close. In fact, it is an accepted dictum that if a thrombus has formed in an arterial segment, it is prima facie evidence of pre-existent atherosclerosis. Often the first evidence of atherosclerosis in any organ is its sudden deterioration following a thrombus in its artery. Myocardial infarction in a previously normally functioning heart and cerebral infarction with mental deterioration in a previously apparently normal brain are well known clinical experiences. Comparative geographic studies also have demonstrated thromboembolic disease is frequent in a population severely afflicted with atherosclerosis, whereas, it is a rarity in a population not similarly involved.[1] From such experiences two obvious questions present themselves. One is, can it be that atherosclerosis itself is but a manifestation of fibrin deposition on the endothelium of arteries? The other is, why is it that clots are prone to form on damaged areas of arteries and veins and not on the normal endothelium?

The thrombogenic origin of atherosclerosis was first proposed by Rokitansky[2] in the middle of the last century. He believed and so stated that fibrin deposit on the endothelium led to "hypertrophy of the membrane" and that the atherosclerotic placque increases in thickness "by addition of new (fibrin) strata." Other changes in the vessel wall such as vascularization, atheromatous softening, hemorrhage and calcification he regarded as secondary processes. Since this was based upon observation, not on experimental verification, it was not difficult for a great figure like Virchow[3] to reject the thesis, essentially because regeneration of endothelium and elastic tissue was not taken into account and because only an enveloping growth from adjacent tissue could produce incorporation of the mural thrombus into the intima. Again, merely supposition replaced experiment which could affirm or deny the fibrin deposition hypothesis. In recent years, Duguid[4] Professor of Pathology, University of Durham, England revived and elaborated Rokitansky's hypothesis. Careful microscopic studies of intimal lesions of human coronary arteries and aorta convinced him that fibrous thickening is the result of vascular organization of mural thromi. "It is not suggested that all atherosclerosis is thrombotic in origin for there are fatty changes to be found in the young aorta which are undoubtedly the outcome of other processes, but it can be shown that most of the features we regard as characteristic of the advanced atherosclerotic lesion including fibrous thickening, hyaline and fatty degeneration atheromatous softening and vascularization of the intima can be products of mural thrombus."

Many workers have subsequently confirmed these observations using electron microscopy and fluoresceinlabelled anti-fibrin antibody,[5] as well as more conventional histologic techniques applied to human tissues. When Friedman and Byers[6] damaged intimas of arteries and followed the evolution of intimal response to injury, they also observed fibrin deposit, its envelopment by intimal proliferation and formation of a placque. It seems clear that thrombosis must be recognized as a factor in the development of atherosclerosis. The problem arises as to what extent such experiments reflect accurately the dynamic processes which normally take place in the formation of atherosclerosis. What about the atheroma that results in rabbits from merely feeding them excess cholesterol? In other words, does the fact that an artery will produce a placque when damaged by a foreign body mean that the formation of all placques depend solely upon a thrombus for initiation, growth or maturation?

If thrombosis precedes atherosclerosis then a general thrombotic tendency should be found in atherosclerosis. In fact, however, there are many instances in which atherosclerosis is not associated with thrombosis. In man, a sizable proportion of myocardial infarction is unassociated with an occlusive coronary artery thrombosis.[7] Numerous studies have attempted to ascertain whether and to what extent changes in the blood coagulation may participate in the development of atherosclerosis and its complications but the results have been quite inconsistent. Some have held that increased coagulability of the blood is present in patients with ischemic heart disease[8] but others did not find it so. When comparing the Bantu with the South African whites. Merskey *et al*[8a] found no evidence to show that "the comparative immunity of the Bantu to severe atherosclerosis and to clinical heart disease is due to a lesser coagulability of the blood." For the present we must accept the fact that augmented clotting tendency and frequency, without attendant changes in intimal disease is an apparent contradiction.

This brings us to our second question, why is it that clots are prone to form on already damaged areas of arteries and veins? That they do is without question. Occlusive coronary thrombosis has been identified as a cause of serious clinical heart disease for at least two generations. During this period, deaths from coronary artery disease have risen steadily in the U.S.A., England and the Scandinavian countries.[9] This progressive change in mortality has generally been attributed to an increasing severity of intimal disease. But Morris[10] points out from a study of postmortem records that it is thrombosis that has increased in frequency while there has been no change in the severity of atherosclerosis.

The proposal that a direct relationship exists between intimal disease and the occurrence of thrombosis seems essential to explain the parallel relationship between severe atherosclerosis and thrombosis. It is interesting to note that almost invariably, complicating arterial thrombi in atherosclerosis involve not the healthy part of the artery but the diseased areas in which the lesions usually are advanced in character. To be sure there are exceptions in which the intimal disease is relatively slight and occlusions have formed despite an intact endothelium. For this reason it has been proposed that the acidmucopolysaccharides of the vessel wall which are most abundant in the intima[11] contribute to the anticoagulant properties of the lining. According to Astrop[12] there is continuous intravascular formation of fibrin from its short lived precursor fibrinogen and the fibrin is quickly lysed by fibrinolytic substances derived from the intima. This would explain why fibrin deposits are not observed over perfectly normal intima.

In atherosclerosis there is a loss of the fibrinolytic substances on the luminal surface of many of the lesions and this could be an adequate explanation for the positional relation of thrombosis. The fact that mural deposits of fibrin are found on the surface of lipid streaks furnishes further evidence of focal loss of clot-inhibiting potency. Such observations would seem to suggest that the abnormal deposits may be a consequence of reduced fibrinolytic activity rather than due to hypercoagulability.

A number of inherent difficulties confront the investigator in making an accurate appraisal of the presence or absence of a coagulative disturbance in atherosclerosis. It is the same problem in almost every other area when methods are not alike. The selection of suitable control groups for comparison is always a serious problem. The significance of observations require cautious and judicious evaluation. The result is, of course, that we must still await final answers to this most perplexing problem.[13]

L.H.N.

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A few have seen their doctor but were assured there was nothing to worry about. If there were complaints, they were "indigestion" or muscle pains. But many are treated in or out of hospitals for varying times before death occurs.

There is a popular notion, often erroneous, that death takes place because of a sudden or sustained exercise beyond the capacity of the heart, such as running for a bus or train. Osborn[1] had only 2 out of several thousand such cases. One was a physician who had had previously an attack of coronary occlusion and was found dead beside a tree he was cutting down. Most have died in bed or during or after ordinary exertion. Motorists with a fatal attack while driving, with very few exceptions, have had enough warning to stop their car at the side of the road.

Death from coronary disease occurs after the disorder in the artery has been present for many years, 10-40 or more. Study of the artery at the end stage reveals an exceedingly complex picture, the result of as many as 35 or more processes. Most of them are irreversible. There is no good reason to believe that biochemical and other findings in the end stages were of importance in the early etiology of coronary artery disease. In many cases (over half) thrombosis did not play any part. If we can't learn too much about coronary disease from the end stages, then can one obtain data from reconstructing the life story of the coronary arteries from birth to death? Perhaps in this way the life story of a coronary artery that has caused death may be determined. For this we would need to learn the state of the coronary arteries at birth and progressively the picture we find at every age until the end-stage.

Osborn[1] carefully studied 465 babies at birth that died of other causes and found all of them had normal coronary arteries. However, by the age of 5 only one-third of the children still had their coronary arteries in the ideal normal stage seen at birth. After age 15 this ideal normality becomes very rare and "dangerous" lesions appear with increasing frequency. Nevertheless some men and women do go through a long life with little or no coronary disease. However, with rare exceptions, the ideal normal structure seen at birth is lost. Even in those men and women who reach an extreme old age without any coronary disease manifest, they all show a little fibrous thickening of the intima. Of course, if some men and women go through a long life and keep their coronary arteries near to normal to the end, perhaps if we knew the reasons why their coronary arteries remained normal we could better search for removable causes in those who die of coronary disease.

The first deviation from normal structure is mucoid infiltration of the intima. Normally the intima should be about equal in thickness with the media and without blood vessels. The internal elastic lamina should show little or no reduplication. The mucoid infiltration — the first sign of pathology seems not to have any effect on the endothelial cells which line the lumen and so the theory that atherosclerosis is due to fibrin deposition on the intima is at once suspect. The mucoid infiltration is not concentric but seems concentrated around the mouth of a branch. Throughout life there is a strong tendency for one segment of the wall of the coronary artery to remain more or less normal. One would suspect that this relationship of the mucoid infiltration at or opposite a branch mouth has a mechanical explanation. The mucoid infiltration shows obvious effects on the subendothelial fibrous tissue. Since it does not affect the artery concentrically, it produces important changes in the shape of the lumen with the production of angles. At these angles the condition of the blood flow is altered and this in turn becomes an important focus in the production of other abnormalities. As the mucoid infiltration and fibrosis progresses it goes on to produce servere gross changes, by which a more or less occluded lumen may be produced without a clot. In fact in Osborn's series 45 out of 86 occlusions were of this type without a thrombus.

The mucoid infiltration not only produces irregularities in the lumen, but invariably it splits the elastic lamina into many thin strands by the mucin. The fragmented elastic fibers then spread through much of the thickened intima where they may either degenerate or proliferate. If they degenerate they provide a source of lipids. If the lumen stabilizes in size for an appreciable time, the elastic fibers which are misplaced in the intima proliferate and may even be successful in forming a new lamina. But since the processes are rarely concentric, the coronary artery is steadily moving to its common abnormal state, in which it has a normal elastic and contractile segment but a large thick and rigid segment.

When the internal elastic lamina is disrupted, it is usually accompanied by important effects on the smooth muscles of the media which are arranged in a circular manner. Large numbers of the nearer smooth muscle fibers are turned inward, now running in different directions radial as well as circular. It appears these smooth muscle fibers have considerable powers of proliferation and spread through the thickness of the intima forming bundles and whorled groups quite like leimyomata, further reducing the lumen. At this stage the intima has become a complex mixture of collagen bundles, mucin, proliferating and degenerating elastic fibers and smooth muscle fibers occurring singly or in tumor masses. This mixture contains nearly all the elements needed to form new blood vessels.

The lipid lesion appears to be appreciably later in development than the mucoid lesion and a higher proportion of people go through life with little or no lipid in their coronary arteries. It is exceptional to find lipids in the coronary artery below age 5. Then it becomes commoner so that by age 16-20 half are affected. The lipid seems first to appear deep in the thickened intima and is free of cholesterol crystals. Lipid then can be seen in foam cells close to the endothelium but is not seen in the segment of the wall that remains normal. There is little doubt that the wall of the artery must be conditioned to receive the foam cells by the earlier mucoid lesions. But the foam cells are a weak part of the wall and must be covered with a thick band of fibrous tissue to avoid rupture, even though this process seriously reduces the size of the lumen. These lesions outlined above, mucin, fractured elastic lamina, overgrowth of smooth muscle and lipid infiltration belong to the "primary process."

The secondary lesions are the most serious, they consist of the development of a secondary blood supply. Obviously when the intima of the coronary artery reaches a certain thickness as a result of the primary processes, parts must either die or develop a supporting blood supply. Apparently there are no deaths from coronary thrombosis unless this happens. Once a secondary blood supply has developed sometimes with surprising speed, small or large hemorrhages are common from the new vessels. The hemorrhages are a source of new lipids. They play an important part in processes which reduce or occlude the lumen. When a hemorrhage has taken place in a pointing atheromatous abscess it is the trigger mechanism for the development of a thrombus. Such a thrombus is usually small, but on it forms secondary thrombi and tertiary thrombi until the lumen is occluded. Atheromatous abscesses were found with or without rupture in 51 out of 86 fatal cases whereas only 41 of the 86 had thrombosis.

Osborn's studies show that most deaths from coronary failure are the result of extensive disease of the artery. As a rule, the processes are very complex but as mentioned above, three major types of lesions are encountered; fibrous strangulation of the lumen found in 50 per cent of sudden deaths; atheromatous abscess in 42 per cent, thrombus in 34 per cent. The last will not develop until the arterial disorder has been present for a long time and a "trigger" mechanism has developed, either a hemorrhage in an atheromatous abscess or as a result of marked turbulence in the vessel, set up by irregular and numerous constrictions.

It is clear that as many as half of the fatal cases do have a lipid factor in their arterial lesion. The lipids are not deposited until the disease of the intima is quite well established, since they never appear to be deposited in a normal intima. But in half of all the cases lipids are of very great importance.

A knowledge of the life story of the coronary artery opens the door to many lines of research. First of all, it is clear that anticoagulants could be of value in less than half of the cases from thrombi. They are useless in others. We ought to search for a way to select the right case for anticoagulation. Perhaps a test for thrombosis at an inapparent site would help. Osborn found evidence that the pathologic processes are phasic in the majority of people. We should try to discover what causes the stops and starts. Then we might prevent established but still silent disease from progressing to the stage of no return.

Most of all those destined to die from coronary disease before their allotted span, owe their fate to lesions of early life not infrequently of infancy. There are a few people who go through life with their coronary arteries almost in a normal state as it was at birth. Infection seemed not to be an important cause. Neither was obesity, nor uncomplicated emphysema. It appears coronary occlusion will be controlled only when we know how to bring every boy or girl to the age of 20 with normal coronary arteries. It is time the pediatricians take a hand in this problem.

L.H.N.

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Blood Coagulation – A Basic Science Review

J. H. Milstone, M.D.

■ In the 30's and 40's the prevailing view of blood clotting was a compromise between the theories of Morawitz (1904) and Howell (1911). Morawitz[1] believed that the activator of prothrombin, which he named thrombokinase, might be an enzyme. Howell[2] thought that this factor was not an enzyme, and he called it thromboplastin. In either case, the "activator" was said to be derived from injured tissue. When blood came in contact with injured tissue this activator, in the presence of calcium, would convert prothrombin to thrombin. The thrombin would then coagulate fibrinogen, with the formation of a solid clot.

It was known in 1905[3] that even after the most thoroughgoing attempts to exclude the juice of injured tissue during collection of blood, it still clotted when it was placed in a glass tube. Upon contact with a glass surface the blood itself became a source of prothrombin activator.

If one wanted to study the activation of prothrombin, he would add reagents such as tissue extracts and calcium and let the mixture incubate. At intervals, a sample of this mixture was added to fibrinogen. The faster the sample clotted fibrinogen, the more thrombin it had. In this way, one could follow the increase in thrombin, to determine how rapidly it occurred, or how much thrombin was produced. These are the essentials of the two-stage test, which is still used as a research method.

Figure I represents the first published two-stage test to show that platelets do not activate prothrombin. The prothrombin was incubated in the presence of calcium in all cases. In the baseline test, platelets were included; and no thrombin was detected for more than an hour. Platelets failed to activate prothrombin, even if they had been broken up; and platelet extracts likewise failed. Platelets do not activate prothrombin which is sufficiently pure. Now if, with those platelets, there was included a small amount of a globulin derivative from plasma, then the two together would activate the prothrombin quite well. On the other hand, if the platelets were left out and only the globulin was included, no thrombin was detected for an hour. As things stood at that time, the activator of prothrombin, as it came from the blood, seemed to depend on both platelets and globulin.

The question which then arose was, which of these two is really the more important activator? Which is primary? Now, extracts of platelets were tried and increasing amounts were added; but there was no thrombin production that corresponded to the increasing quantities of platelet extract. On the other hand, Fig. II shows that when the globulin factor was purified and concentrated, it could activate the prothrombin all by itself without the help of platelets and without the help of calcium ions—even in the presence of oxalate. This is not entirely surprising. There are many circumstances where prothrombin is activated in the presence of calcium-binding agents; and we know in particular, that the pancreatic enzyme, trypsin, can activate prothrombin in the presence of oxalate just as thrombokinase does here. Once the globulin factor was found to be the prime activator, it was identified as thrombokinase, activator of prothrombin. Fig. II also shows that the rate of activation is proportional to the amount

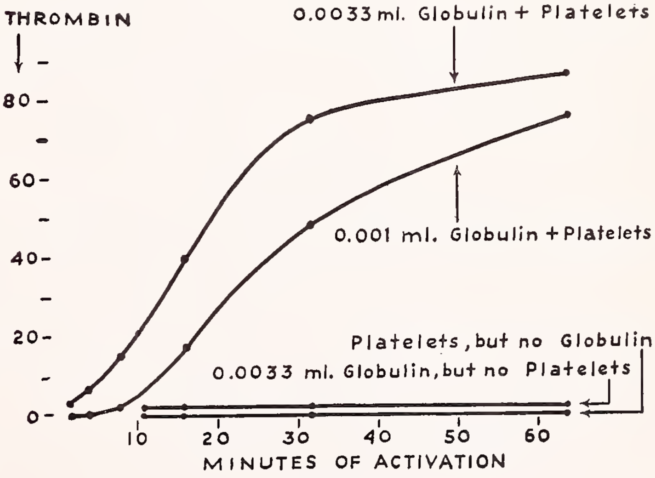

FIGURE I

All tests contain prothrombin, which can be activated by globulin plus platelets, but not by platelets alone. Ionic calcium is included in all these tests. Figure taken from reference 4.

Presented as a scientific program of the regular monthly meeting of the Bridgeport Medical Association, November, 1961. All papers have been re-edited and brought up to date. (Some of the work described in this article was supported by Research Grant H-3906 from the National Heart Institute Public Health Service.)

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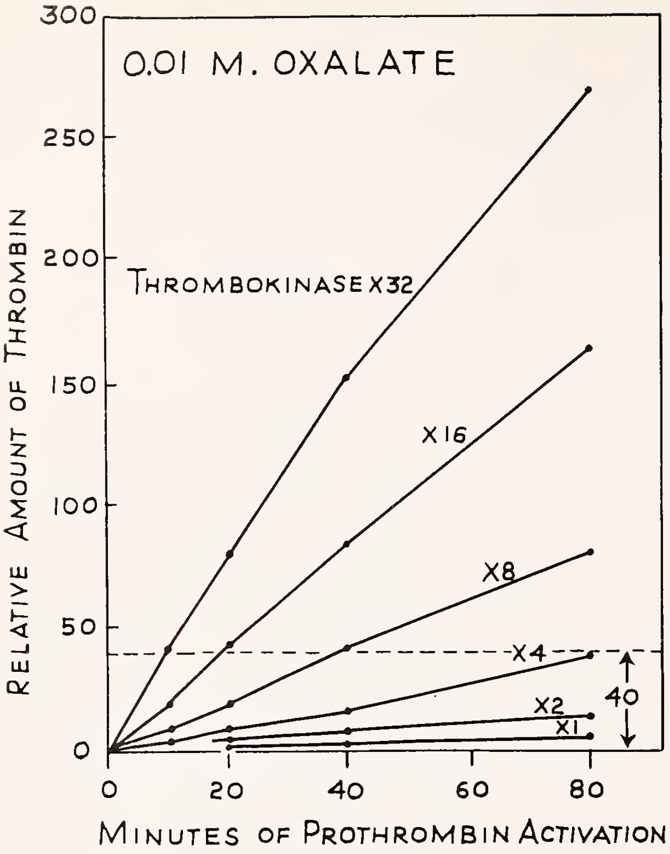

Figure II

The globulin factor, when sufficiently concentrated, can be identified as thrombokinase, activator of prothrombin. Tests contain prothrombin, oxalate and varying amounts of thrombokinase. Chart drawn from data which were tabulated in reference 5.

of thrombokinase. This fact, too, is consistent with the view that thrombokinase is a trypsin-like enzyme.

Production of thrombin without calcium ions seems to be inconsistent with what occurs in whole blood. But the amount of thrombokinase which is available in blood is comparatively small; and it will activate the prothrombin only very slowly, when it acts on prothrombin alone. However, when calcium and platelets are present with the prothrombin and thrombokinase, activation occurs rapidly, as seen in Fig. III. It is of further interest to note that if platelets are included, but no calcium ions, the platelets have no significant effect. In other words, the platelets do not exert their accessory effect unless they are accompanied by calcium ions.

This was done with purified materials. In the course of preparing these materials, most of the physiologic anticoagulant mechanism was eliminated. However, in the presence of much normal anticoagulant, basic relations are obscured. In whole blood, citrate can tie up the calcium ions and thereby prevent platelets from acting. Then the unaided action of kinase is so slow, and the anticoagulant mechanism so effective, that a gross clot never forms.

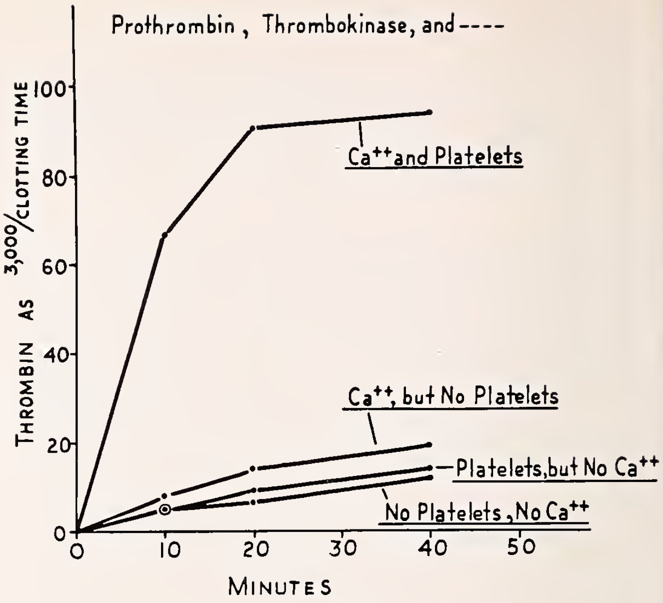

Figure III

When both prothrombin and thrombokinase are present, platelets exert an important accessory effect. For this effect ionic calcium is required.

Although thrombokinase is obtainable from blood only in small amounts, it is potent. When it is purified, it can be measured at a concentration of a thousandth of a microgram per ml. But, correspondingly, not much is needed to get a physiologic effect; and not much is obtainable from blood. We get only a small amount. 738 liters of bovine plasma were used to prepare the throm-

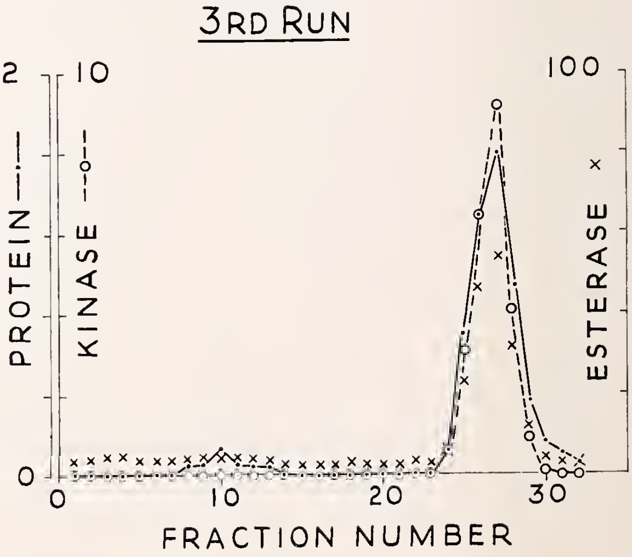

Figure IV

Thrombokinase has been isolated by repeated electrophoretic fractionations. It is now identifiable as an enzyme with esterase as well as thrombokinase activity. Figure taken from reference 6.

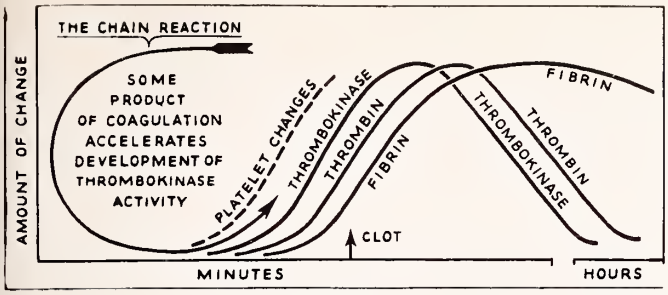

Figure V

Diagram of the dynamic aspects of blood coagulation. Figure taken from reference 11.

bokinase that was analyzed in Fig. IV. This analysis was done by continuous paper curtain electrophoresis so that individual fractions could be taken and analyzed separately. As is shown by the dotted curve there is a slight hump at fraction 10. Otherwise, all the protein occurs in one single spike, showing that the protein is almost homogeneous under the conditions of this test. The tests for kinase, represented by the circles, have a correspondingly sharp peak, which gives strong indication that the purified kinase is the same as the purified protein. Finally there are tests for esterase action on the synthetic substrate, TAMe. These show that the esterase activity is parallel to thrombokinase, and probably a property of the same molecule. That is, thrombokinase protein is an enzyme which not only activates prothrombin but also has an esterase action on the particular subtrate. Trypsin has a very strong action on the same substrate. And this is one more indication that thrombokinase is a trypsin-like enzyme.

According to these experiments, platelets and calcium ions are important accessory factors for the enzymatic action of thrombokinase. Quick[7] was one of those who long ago suggested that prothrombin activator is derived from plasma, and not from platelets. Quite recently, Macfarlane[8] has proposed that prothrombin activator is produced by a series of reactions which involve the clinically-recognized plasma factors in the following order:

XII (Hageman)
XI (PTA)
IX (PTC)
VIII (AHF)
X (Stuart)
V (Proaccelerin).

Resemblances have been noted between the activated form of Factor X and thrombokinase[9]. And thrombokinase preparations have shown high activity in laboratory tests for Factor X (Nemerson, Spaet, personal communications). These comparisons have aroused speculation that these two factors, defined in different ways, might actually be identical. And renewed attention has been focussed on the question, whether Factor V represents an accessory factor or a source of more thrombokinase[10]

Meanwhile, the classical concept of tissue factor is also being revised.[8] However, if we consider only the factors of the intrinsic clotting system, we see in Fig. V how they fit into a larger scheme of events. During the clotting of blood, there is a set of platelet changes which manifest themselves in two main ways. For one thing, the platelets become sticky. They stick to their surroundings; they stick to each other. They help to form a hemostatic plug. For another, they contribute to thrombokinase activity. Three sets of reactions occur in the plasma; and for each wave of reaction, there is a corresponding dynamic counter-action, which tends to remove the product. For the thrombokinase wave, there is the anti-kinase effect; for the thrombin wave there is the antithrombin effect. For fibrin there is a fibrinolytic effect, which under ordinary circumstances is slow. Instead of resembling a bomb that goes off when a button is pressed, the clotting system is more like a fire that is always smoldering in the circulation, ready to burst into flame when it is fanned. Finally there is a chain reaction in which some product of coagulation works early in clotting and accelerates the development of more thrombokinase activity. As a consequence, a little bit of clotted blood tends to make more blood clot. This effect may contribute to the growth of a hemostatic plug and to the propagation of a thrombus. This is a bare outline to serve as a basis for discussion. From the scientific viewpoint, we can consider that a half century ago progress was blocked at the question of what activates prothrombin; and that point is now yielding. But, meanwhile our clincial colleagues have added many new observations which must be built into our theoretical structure.

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Reports Of Medical Cases, With Reference To Morbid Anatomy
Preface By Richard Bright—1827

One great cause of dropsical effusion appears to be obstructed circulation; and whatever either generally or locally prevents the return of the blood through the venous system, gives rise to effusions of serum more or less extensive. Thus, diseases of the heart which delay the passage of the blood in the venous system, give rise to general effusion, both into the cavities and into the cellular tissue. Obstructions to the circulation through the liver, by causing a delay in the passage of the blood through the veins connected with the vena portae, give rise to ascites. The pressure of tumours within the abdomen preventing the free passage of blood through the vena cava, gives rise to dropsical effusion into the cellular tissue of the lower extremities; not not unfrequently, the obliteration of particular veins from accidental pressure is the source of the most obstinate anasarcous accumulation. . . .

There are other appearances to which I think too little attention has hitherto been paid. They are those evidences of organic change which occasionally present themselves in the structure of the KIDNEY; and which, whether they are to be considered as the cause of the dropsical effusion or as the consequence of some other disease, cannot be unimportant. Where those conditions of the kidney to which I allude have occurred, I have often found the dropsy connected with the secretion of albuminous urine, more or less coagulable on the application of heat. I have in general found that the liver has not in these cases betrayed any considerable marks of disease, either during life or on examination after death, though occasionally incipient disorganization of a peculiar kind has been traced in that organ. On the other hand, I have found that where the dropsy has depended on organic change in the liver, even in the most aggravated state of such change no diseased structure has generally been discovered in the kidneys, and the urine has not coagulated by heat. I have never yet examined the body of a patient dying with dropsy attended with coagulable urine, in whom some obvious derangement was not discovered in the kidneys.—*Original Papers of Richard Bright on Renal Disease.* Edited by A. Arnold Osman. London, Oxford University Press, 1937, p. 1.

The Bleeding Patient

Martin C. Rosenthal, M.D.

■ It was a pleasure to hear Dr. Milstone present his material and indicate something that, I think, most of us lose sight of, namely, that clotting is always going on. The body is constantly removing and renewing clotting factors. At times we accelerate the process by some procedure through loss of factors and activation of others. The coagulation system is such a delicate one that it can be easily disturbed at times through genetic mechanisms or by acquired mechanisms.

Of course, no one likes a bleeding patient. The surgeon doesn't like it, the family doesn't like it, and the patient certainly doesn't relish it. An event that should be routine suddenly becomes a rout. At times, such a disaster may be averted by preoperative investigation of the patient. The preoperative screening of patients for any bleeding tendency has been more or less something of a bugaboo, especially to the clinical pathologist. A few years ago, Porter and Diamond, and I think the rest of us, had indicated to our hospitals that the ordinary clotting profile, as it is done for the preoperative patient, is completely inadequate. To do a simple bleeding time and a capillary clotting time, which are gross tests, rarely uncovers anything in a system as delicate as blood coagulation. It is of far greater importance to question the patient and take a careful history. (Table I) Family histories are very important, as are previous bleeding episodes, especially in circumcisions, dental extractions, tonsillectomies, gynecological operations, and abnormalities in menstrual periods. These are apt to give the clue as to whether the patient has some type of inherent coagulation defect. If an individual gives a history of bleeding from various sites, that too calls for investigation. The individual who is on medication or who is an alcoholic or who has a grossly deficient diet may also be a candidate for clotting deficits.

I would urge everybody to listen to the patient who states that he is a bleeder. There are many people who get shunted from laboratory to laboratory claiming they are bleeders and about whom nothing is discovered. With the passing of time our laboratory tests have improved, and many of these patients have been verified to have coagulation defects. The patient has to be given a good deal of credence when he says that he or other members of his family are bleeders. This is a real danger signal, especially if he states that on prior dental work, such as ordinary gingival scraping or dental extraction, bleeding had occurred. In addition, physical examinations are important and evidence of petechiae, ecchymoses, jaundice, and other finding that we are well acquainted with are all indi-

TABLE I
HISTORICAL DANGER "ALERTS"

1. FAMILIAL HISTORY
2. PREVIOUS BLEEDING EPISODES, CIRCUMCISION
   DENTAL
   TONSILLECTOMY
   GYM. & OTHER
3. MULTIPLICITY OF SITES
4. DIET, DRINK, DRUGS

TABLE II
PHYSICAL DANGER "ALERTS"

1. PETECHIAE AND ECCHYMOSES
2. JAUNDICE
3. GINGIVAL CHANGES
4. ADENOPATHY
5. HEPATO-SPLENOMEGALY
6. TELANGIECTASIA
7. JOINT CHANGES
8. PROSTATIC FIRMNESS

TABLE III
A "ROUTINE" COAGULATION SCREEN

1. TOURNIQUET TEST
2. BLEEDING TIME (VENOUS)
3. COAGULATION TIME (IVY)
4. CLOT OBSERVATION
   a. RETRACTION
   b. LYSIS
5. PROTHROMBIN ACTIVITY OF PLASMA
6. PROTHROMBIN ACTIVITY OF SERUM
7. FIBRINOGEN LEVEL
8. PLATELET COUNT AND/OR SMEAR
9. PARTIAL THROMBOPLASTIN TIME

ABOVE TESTS DELINEATE AREA FOR FURTHER INVESTIGATION.

From the Department of Hematology, The Mount Sinai Hospital, N.Y. Aided by Grants from the Albert A. List, Frederick Machlin and Anna Ruth Lowenberg Funds, Metropolitan Chapter, National Hemophilia Foundation and National Hemophilia Foundation.

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cations for the performance of some type of coagulation work-up prior to any operative procedure (Table II).

If we do have to perform laboratory studies, what would constitute an adequate investigation? Table III indicates the routine coagulation screen that we use on preoperative patients if there is an indication, that is, in those individuals where the history or physical examination indicates that there might be some reason for concern. Economically and from the standpoint of time, such a work-up takes several hours, and would be completely impossible to do on every preoperative patient. When this type of procedure is performed it does not mean that it, in itself, will uncover a defect. A procedure of this type may indicate a certain area that requires further investigation or, if this fails to uncover anything and the individual still is suspected of having a bleeding tendency, then we proceed to do some elaborate tests. All of this takes considerable time and effort but it is well worthwhile if you can prevent a patient with a true coagulation defect from being operated upon.

When one uncovers a patient with a coagulation defect who does require an operation, obviously this patient has to be prepared. It is impossible to go through the preparation of patients who have various coagulation defects, but briefly it involves a knowledge of the material for replacement of the deficient clotting protein. One should know its natural life span in order to time the administration of the replacement therapy. It is necessary to have some idea of how that individual patient handles the material, because occasionally you not only have a coagulation defect but also the appearance of anti-clotting factors as well. Therefore, it is incumbent upon the individual preparing the patient to know the physiology of that clotting factor.

Occasionally a patient who is on Dicumarol® or Coumadin® requires a sudden operation. This patient has an acquired coagulation defect and it is a rather complex one. It does not involve prothrombin alone; it involves factor VII, factor X, and even one of the factors in the first stage of coagulation, factor IX. The administration of vitamin K is necessary but not all preparations of vitamin K are helpful. One has to give a specific, such as Mephyton.® Other synthetic vitamin K preparations are not effective in the preparation of a patient who has previously been on anti-coagulant therapy. In addition, it has to be recognized that there is a lag phase, which takes at least four to eight hours before that individual can be subjected to an operation. If immediate operation is necessary, then replacement therapy in the form of plasma must be administered. It need not be fresh plasma, since banked plasma will sufficiently restore the prothrombin and other factors in that individual to permit operation.

TABLE IV
THE UNRECOGNIZED BLEEDER

LITTLE OR NO FAMILY HISTORY
NO PRIOR SURGERY
NO "SPONTANEOUS" EPISODES
TURNS OUT TO BE:
1. MILD AHG, PTC, PTA DISEASE
2. MILD PSEUDOHEMOPHILIA
3. UNRECOGNIZED THROMBOCYTOPENIA
4. UNRECOGNIZED LIVER DISEASE

TABLE V
DANGER ALERTS ON THE POST-OP PATIENT

1. DRUGS
    ANTIBIOTICS
    TRANQUILIZERS
    COUMADIN ETC.
2. TRANSFUSIONS
3. OPERATIVE DETAILS
    LENGTH OF SURGERY
    SITE OF SURGERY
    TIME OF BLEEDING

Now, what about the patient who is operated upon and who bleeds? He may not have a family history or a past history which would serve as a warning sign. Approximately half of the patients with inherited defects give no family history. Unrecognized bleeders in our experience have defects in the first stage of coagulation (Table IV). It is very common for me to come across a patient who states that he is 55 years old and has had many operations, all of them most unsatisfactory from the hemostatic viewpoint. It is difficult to detect such mild deficiencies but with newer tests one can uncover these defects.

Pseudo-hemophilia is a bleeding defect in which the beeding time is the only abnormality. Of course, there yet remain patients with unrecognized thrombocytopenia, especially women with menstrual difficulties and individuals with liver disease.

In addition to patients who have a clotting liability that is completely unknown and who happen to be operated on, postoperatively a perfectly normal individual may develop certain clotting defects. On these postoperative patients, who seem to do well until they are operated upon and then start to bleed, there are certain things that we routinely investigate. One factor is drug therapy (Table V). Either long-term antibiotic therapy, or intensive short-term antibiotic therapy in certain individuals, especially in children either prior to operation or postoperatively, can deplete the body very rapidly of vitamin K and cause severe hypoprothrombinemias. Antibiotics, such as streptomycin and chloramphenicol can cause thrombocytopenia. Occasionally individuals are operated on who have been on anticoagulant drugs and fail to tell anybody of this.

Another cause for postoperative bleeding may be prolonged surgery, especially involving brain, lung or pancreas. Occasionally we encounter neurosurgical patients who seem to do well initially but, as they go along, start to ooze slightly. It is realized that an alteration in hemostasis has occurred and a fibrinolytic mechanism is involved. The time of the bleeding is diagnostically important. The individual who bleeds immediately upon incision has pre-existing defect whereas the delayed bleeder has an acquired defect.

Transfusion induced bleeding may occur if incompatible blood has been given. Such a reaction may go undetected during anesthesia. A complex type of coagulation defect develops in which thrombocytopenia, a fibrinogen deficit and a prothrombin deficit, exists. Similarly contaminated blood, especially with gram negative organisms, can cause a transfusion reaction which may be followed by a complex hemostatic defect. The commonest type of transfusion-induced bleeding is seen following massive blood transfusions. The administration of five to ten units of blood within a 24- to 48-hour period almost uniformly causes severe thrombocytopenia and this may be followed by clinical bleeding. The exact cause for this thrombocytopenia is unknown. It has been suggested that banked blood, being poor in platelets, causes a dilutional type of thrombocytopenia to develop. Other theories suggest platelet incompatibility, platelet damage or some type of platelet destroying factor as the basis for such thrombocytopenia. Even one transfusion may result in a distinct reduction in the platelet count. There seems to be something inherent in banked blood which will do this. Krevins has indicated that fresh blood will prevent this thrombocytopenia, but this may not always be the case.

Calcium depletion probably never arises as a cause of bleeding following massive transfusions. However, in general, we have a rule that for every ten units of citrated blood that is rapidly infused, it is best to give 5 to 10 cc. of calcium gluconate very slowly primarily to prevent convulsive disorders as a consequence of citrate binding.

One other word about massive blood replacement. Occasionally when there is not enough blood, one may resort to Dextran. Dextran being a synthetic material of high molecular weight may, after a certain amount is given, cause a bleeding diathesis. The exact nature of this bleeding diathesis is obscure, but it is felt to be either due to coating of the platelets or interference with the conversion of fibrinogen to fibrin.

TABLE VI
HYPOFIBRINOGENEMIAS OF PREGNANCY
ETIOLOGY

1. PREMATURE SEPARATION
2. AMNIOTIC FLUID EMBOLIZATION
3. RETAINED DEAD FETUS
4. TOXEMIA
5. SEPTIC ABORTION

Bleeding in post-partum patients is always exceedingly trying, and I would like to give an illustration of a case and its complexities. A 41 year old woman had a placenta praevia. Bleeding occurred and it was recognized that she had a low implantation. She was taken to the operating room and a Caesarian section was performed with manual removal of the placenta. Upon returning from the operating room she continued to bleed; obviously she was not doing well so she was taken back to the operating room, given blood and a hysterectomy was performed. She was brought down again, continued to bleed and this time a coagulation workup was done by the obstetrical resident, who discovered that the clotting time was somewhat prolonged. In addition, as he observed the clot, it lysed almost immediately. I was called in and by this time the woman had received 10 units of blood. Levophed® was being used to combat shock. With difficulty, blood was obtained from the patient and the clotting defect confirmed. Fibrinogen was administered, as well as fresh blood, but she continued to do badly. By this time, the patient had a normal fibrinogen level grossly and the blood clotted normally. The surgeon, on hearing this, promptly took the patient to the operating room, re-explored her (the third operation in about four hours), and removed a cervical stump that was wide open and obviously bleeding. Such a situation requires a great deal of judgment. If one persisted in focusing on the coagulation abnormality, this patient would have died. Fortunately, the surgeon had enough courage to feel that if the coagulation defect had been corrected, and the patient continued to bleed, there must be a local site for hemorrhage.

At one time, hypofibrinogenemia in pregnancy was a rare diagnosis. Now it may be over-diagnosed.

TABLE VII
HYPOFIBRINOGENEMIAS OF PREGNANCY
PATHOGENESIS

1. FIBRINOLYSIS
2. DEFIBRINATION
3. LOSS OF UTILIZATION
4. ALTERED REACTIVITY

Uterine atony, lacerations of the cervix, and other obstetrical problems still cause hemorrhage. They have to be considered. The hypofibronogenemias of pregnancy can have various etiologies, as indicated in Table VI. Theories for the pathogenesis of hypofibrinogenemia are outlined in Table VII. The fibrinolytic system (the plasminogen-plasmin system) involves fibrinogen, fibrin, and other clotting factors as well. Massive release of thromboplastic material into the circulation may occur leading to intravascular clotting. What is circulating is not plasma but is, in a sense, serum. It is low in platelets, low in the first stage factors, prothrombin, labile factor and fibrinogen. If one tests the plasma it behaves as if clotting has occurred. There are other theories, namely, that the developing hematomas utilize the fibrinogen and remove it from the circulation. Another theory suggests that the fibrinogen is normal, but is changed in its reactivity and does not respond to thrombin in the normal fashion.

The most dramatic form of hypofibrinogenemia is amniotic fluid embolization. A sudden catastrophic event occurs. Before any evidence of bleeding, these patients develop a shock-like state. Bleeding starts, and we feel that such patients have had massive amounts of thromboplastin released into the circulation. This causes the fibrinogen to be converted into fibrin and that the shock then activates fibrinokinase which in turn activates the fibrinolytic system making the situation a self perpetuating affair. It starts out bad but matters get worse very quickly. In order to cope with this situation, it is necessary to break up the cycle in some way and the first measures consist of combatting shock. This is treated with large quantities of blood using fresh blood if possible. In addition to hypofibrinogenemia, these patients have thrombocytopenia and are low in other elements. In addition, routine anti-shock measures are used. Included also in our routine is the administration of intravenous steroids, because massive infarction of the pituitary or massive adrenal hemorrhage may occur. Fibrinogen is given in initial doses of 4 gm. followed every 20 to 30 minutes by an additional 4 gm. until the clot is firm. With such a regimen, most of the patients can be carried through whether they have premature separation of the placenta, toxemia of pregnancy, or amniotic fluid embolization. A certain number of patients will be lost simply because one cannot cope with the situation. If hypofibrinogenemia develops before delivery, one must treat the coagulation defect before any active measures take place to deliver the baby. Occasionally if uterine atony occurs secondary to shock, hysterectomy may be required but only after control of the bleeding tendency.

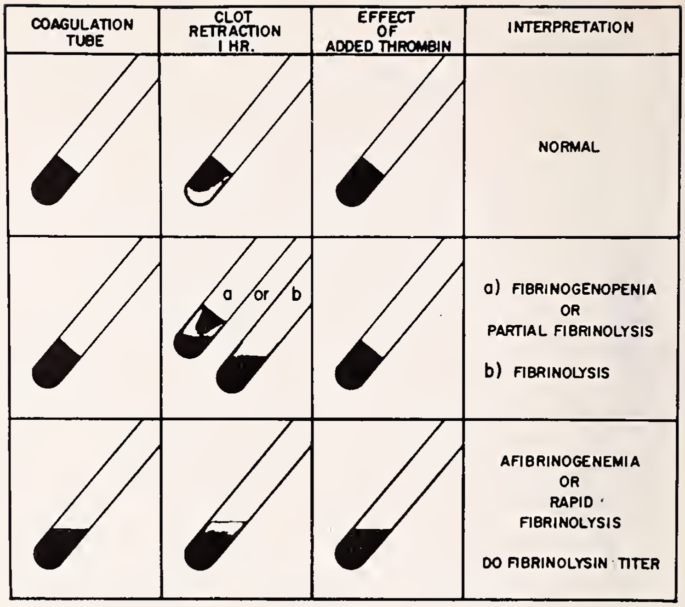

Figure I

For the detection of hypofibrinogenemia, we use a very simple method utilizing the clotting time plus a thrombin clotting time (Fig. I). Normally a firm clot is formed with retraction soon afterwards. If thrombin is added to whole blood, it will clot within 3 to 5 seconds. If the patient has a fibrinogenemia that is complete, the blood remains liquid with or without added thrombin and no clot is formed. If a low fibrinogen exists, a small "nubbin" of clot forms with untrapped red cells. It then may lyse completely within a few seconds, if there is an additional factor of fibrinolysis.

There are other conditions in which fibrinolysis is important. In metastatic carcinoma of the prostate, a fibrinolysin may develop which will cause a bleeding diathesis. The fibrinolysin supposedly comes from prostatic tissue. In carcinoma of the prostate, the fibinolytic purpura that develops is very capricious. It will come and it will go. It will respond to estrogens and sometimes it will respond to steroids. It will at times be self limited. Consideration of an orchictectomy to control the situation is out of the question because one would then have to cope with an exsanguinating hemorrhage. Fibrinogen may be given but many times therapy with estrogens alone may be sufficient. A similar syndrone may occur with other neoplasms. It has been seen with carcinoma of the colon, carcinoma of the stomach, carcinoma of the gallbladder with, however, metastases to the bone marrow usually being present. The etiology is unknown.

There are many other situations that play a role in postoperative bleeding. Occasionally, one runs into polycythemics that are operated on who bleed severely. This type of bleeding is completely mysterious. Patients who have been taking salicylates may exhibit gastrointestinal hemorrhage. Some of these individuals may have a coumadin-like action due to the salicylates, but this is extremely rare and it is more or less due to an individual idiosyncrasy. Others have increased capillary fragility due to salicylates. Some are truly sensitive to the drug *per se,* but by and large, the bleeding from salicylates is due to an erosive gastritis which causes the bleeding.

As a hematologist I am often asked what is a universal antidote for bleeding? The only universal antidote that is known is fresh whole blood. Blood contains everything that is possibly needed. If a plastic bag system is used it will even contain a fair amount of platelet thromboplastic material. This is the universal antidote. It is still worth emphasizing that patients may bleed from open blood vessels and no amount of "coagulant material" can be given to a patient which will stop hemorrhage from an open blood vessel. The management of a bleeding patient requires a great deal of cooperation between the laboratory and the clinician who has the responsibility of patient care. The laboratory can help in trying to rule out a bleeding disturbance but the physician's judgment is still important.

Presented as a scientific program of the regular monthly meeting of the Bridgeport Medical Association, November, 1961. All papers have been reedited and brought up to date.

Conjectures And Some Conclusions

Now a few things about the nature of animal electricity chosen from those which it is permissible to infer from the described experiments. This electricity, then, has some things in common with artificial and with ordinary electricity, some things with that of the torpedo and other animals of this class.

Things in common with ordinary electricity are: First, free and easy passage through the same bodies through which common electricity is accustomed to pass, namely through metals, among the foremost and, among these, through the more perfect and nobler, such as gold and silver, then through the less noble, namely copper, iron, tin and lead, moreover through the imperfect metals, such as antimony, and finally through minerals; likewise free and easy passage through water and moist bodies; more difficult passage through stones, earth, and wood; finally, interrupted and completely cut off through glass, resin and oily substances: wherefrom it results that if metals are laid on an insulating plane, it is inevitable that common and artificial electricity should accumulate in them, and they would be wont to produce far greater effect, namely to excite more violent and longer contractions, than if the same metals communicated freely with other conducting bodies.

Second, the choice, in excursion, of a shorter and quicker way, an arc, for example, or angles, or points.

Third, a double and opposite nature, namely one positive, the other negative.

Fourth, daily and hourly constant attachment to muscles not otherwise than common electricity is wont by nature to electric bodies.

Fifth, spontaneous restoration, not lasting a short space of time.

Sixth, distinct increase of power by employment of the device of a so-called armature made of the same metal with which the physicists are accustomed to surround resinous and vitreous bodies.—Luigi Galvani. *Commentary on the Effect of Electricity on Muscular Motion.* Translated by Robert Montraville Green, M.D. Cambridge, Massachusetts, Elizabeth Licht, Publisher, 1953, p. 65.

Fibrinolysis

Dionysios Adamis, M.D., Ph.D.

■ Since the time is getting late, I am going to talk briefly on another aspect of coagulation, fibrinolysis, which is closely related to both abnormal hemorrhages and thrombosis. As you probably know, the first observation of fibrinolysis was made by Morgagni[1] 200 years ago. He observed that blood from patients who have had a sudden death did not clot. The term fibrinolysis was introduced by Dastre[2] 132 years later, and almost in the same year Danys noticed that when chloroform was mixed with serum, proteolytic activities were exhibited. In 1933, Tillet and Garner[3] found that filrates of streptococcus hemolyticus exhibited fibrinolytic activity when mixed with blood. In 1937 MacFarlane[4] noticed that after major operations, the fibrinolytic activity of blood was moderately increased. He noticed also with Biggs[5] 10 years later that after severe exercise or after the injection of adrenalin, the fibrinolytic activity of blood was greatly increased.

The phenomenon of fibrinolysis was considered as an abnormal one, but it was shown by Fearnley and Tweed[6] that it occurs in every normal blood. According to their tests, if plasma is diluted 1:10 under certain conditions, and clotted with thrombin, fibrinolysis occurs within 4-5 hours at 37° C.

The mechanism of fibrinolysis *in vivo,* despite the accumulated knowledge in the last decade, is still not completely clear. It is known that plasminogen (profibrinolysin) is converted to the active enzyme, plasmin, by different activators. These activators are found in tissues (tissue activator) or in plasma (plasma activator) or in urine (urokinase). Activators have also been isolated from cultures of different bacteria (streptococcus, staphylococcus, etc.). The activation of plasminogen to plasmin can also take place through a different mechanism in vitro by means of chloroform or glycerol. An excess of these activators can produce fibrinolysis or more correctly, proteolysis, in the presence of plasminogen (Figure 1).

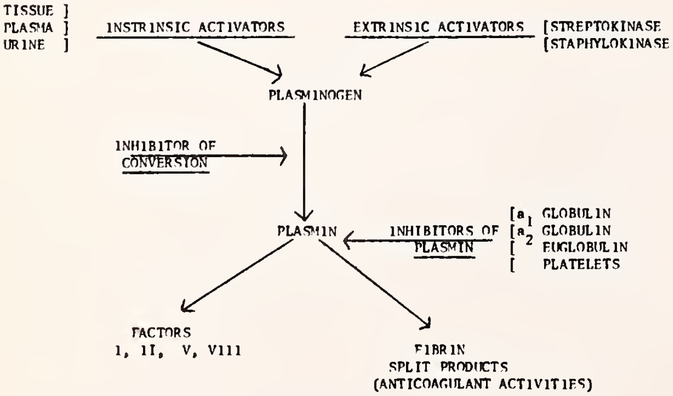

FIGURE 1

The fibrinolytic mechanism in vivo, and in vitro.

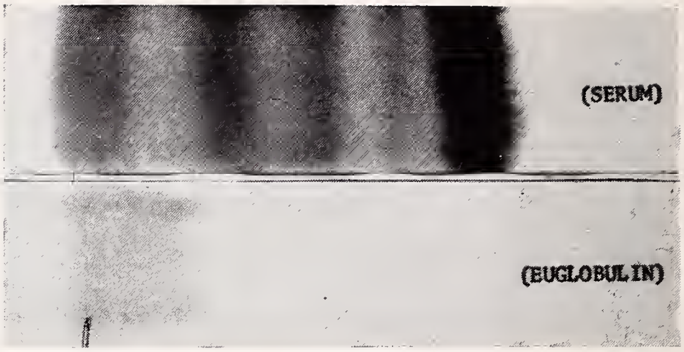

FIGURE 2

Electrophoretic pattern of human serum and of the euglobulin fraction: The latter does not contain the a_1 and a_2 globulins, however, it possesses considerable antiplasmin activity as is shown in Figure 3.

On the other hand, other mechanisms counteracting the fibrinolytic ones were detected in normal blood. They can be divided into two groups:

(1) Inhibitors of plasminogen activation. These have not been completely studied. However, evidence of their presence was given independently by Jacobson[7] and Mullertz.[8] Evidence of this inhibitor was obtained in our laboratory recently, and the experimental data will be published shortly.

(2) The second group of inhibitors concerns those of plasmin. Two distinct inhibitors designated as a_1 and a_2 have been studied extensively by Norman.[9] They migrate with the a_1 and a_2 globulins in plasma electrophoresis. In our Research Department, it was found that another inhibitor was contained in the euglobulin fraction (obtained according to the Milstone technique). The activity of this inhibitor can be demonstrated if the euglobulin fraction is previously heated at 56° C. for 30 minutes. By electrophoresis, the euglobulin fraction does not contain any a_1 or a_2 fractions as is shown in Figure 2. This proves that antiplasmin

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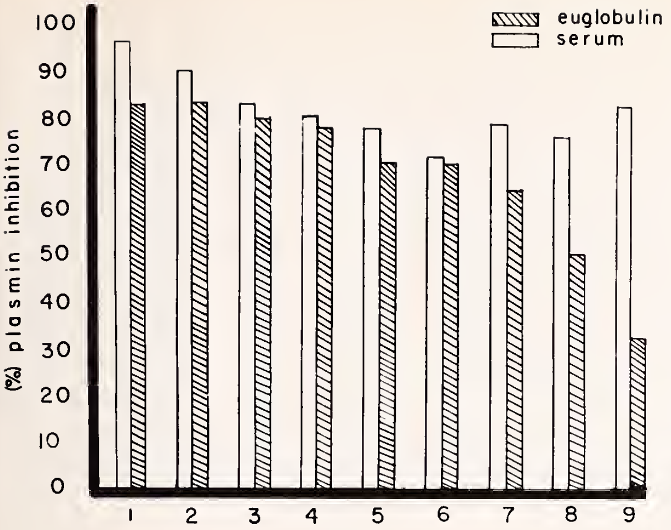

FIGURE 3
The antiplasmin activity of the serum, and of their euglobulin fractions in 9 patients. Both samples were preheated at 56° for 30 minutes and then tested for inhibitory activity according to the antiplasmin test shown in Figure 4.

contained in the euglobulin fraction is completely different from the ones described: a_1 and a_2.

These results with a new technique for the determination of antiplasmin (Figures 3 and 4) were presented at the Federation Societies for Experimental Biology.[10] The two systems of plasmin activators and inhibitors are in balance in normal individuals. It seems that they protect blood from both hemorrhage and thrombosis. It is believed by Astrup[11] that a continuous deposition of fibrin occurs in the vascular wall and also that there is continuous lysis through fibrinolysis. This theory of the hemostatic balance can explain many abnormal conditions of both thrombosis and hemorrhage. Actually, this hemostatic equilibrium depends on the balance between activators and inhibitors. Any predominance or deficiency of one of them can result in thrombosis or hemorrhage. However, this theory does not cover completely the etiology of hemorrhages or thromboses. From a clinical point of view, hemorrhage due to fibrinolysis has been noticed occasionally in the following conditions.

a. In obstetrical complications of abruptio placenta, intrauterine retention of a dead fetus and amniotic fluid embolism.
b. In carcinomas of the prostate.
c. After pulmonary surgery.
d. After extensive burns or trauma.
e. In hepatic cirrhosis, in leukemia and polycythemia.
f. After prostatectomy.

In some of the above conditions, it is thought that the tissue activator is circulating in the blood because of the injury; however, increased fibrinolysis has been noticed without injury.

The treatment of hemorrhages due to fibrinolysis consists of several transfusions of fresh blood or administration of 4-8 grams of human fibrinogen. Some criticism was raised recently against administration of fibrinogen, since the split products due to fibrinolysis possess anticoagulant properties. This will be explained later.

I would like also to emphasize that during the state of fibrinolysis, not only is the level of fibrinogen markedly or completely decreased (afibrinogenemia), but that other coagulation factors are affected, especially factors V, VIII, and prothrombin. In addition, it was found that some fractions of the split fibrinogen possess anticoagulant properties, which further inhibit the action of thrombin on fibrinogen. Thus it appears that hemorrhages due to fibrinolysis, in nature, are not as simple as we thought a few years ago.

Lately we have had the opportunity to study an obstetrical case of fibrinolysis with severe hemorrhage. It was found that the inhibitors of plasmin were extremely low. Perhaps the deficiency of inhibitors was the initial cause of developed fibrinolysis. The patient recovered after several transfusions of fresh blood. I think that a complete study of both sides of the fibrinolytic mechanism in states of abnormal fibrinolysis would give a more profound understanding of its etiology. The determination of fibrinogen level, though helpful in the diagnosis, does not explain the etiology of fibrinolysis. On the contrary, in another special group of hemorrhages (concerning patients undergoing prostatectomy) the cause of fibrinolysis was found and subsequently treatment was rather successful. It is believed that urokinase, which is con-

ANTIPLASMIN TEST

Plasmin Reagent	0.5 ml	15'/37° C
Serum Tested	0.1 ml	
Fibrinogen (150 mgs %)	1.0 ml	
Thrombin (in 0.1 ml)	50 NIH Units	
Lysis Time, 37° C		

FIGURE 4
Description of the antiplasmin test. In a standard amount of plasmin reagent is added 0.1 ml. of the sample containing the antiplasmin to be tested and incubated from the clot lysis time, upon the addition of 1.0 ml. of fibrinogen solution (0.3 per cent) and thrombin. The samples to be tested are pre-incubated at 56° C. for 30 minutes.

tained in urine, activates plasminogen found in thrombi covering the injured surface of tissues during prostatectomy, thus producing local fibrinolysis which results in hematuria. In these patients the administration of 6 to 10 grams of epsilon-aminocaproic acid is the treatment of choice, since it is an inhibitor of both plasmin and plasminogen activation.

The Use Of Fibrinolysis In The Treatment Of Thrombosis

The process of fibrinolysis resulting in hemorrhage is obviously considered an abnormal condition. Various investigators tried to induce fibrinolysis in experimental thrombosis. Encouraged by their results they induced fibrinolysis in clinical thromboembolism. Thrombolysis can be achieved by two methods; by injection of a strong activator, i.e., streptokinase, or by injection of activated plasminogen (plasmin). Some investigators preferred the first agent, and some the second. The pharmaceutical companies producing fibrinolysin preparations produced a mixture of a known number of plasmin units with an unknown number of streptokinase units. Both groups reported enthusiastic results in the beginning. Today, after some years of experience, the results are not extremely impressive. In some cases the symptoms of thrombosis disappeared dramatically, but they reappeared within 24 hours.[12] However, there were reported cases of thromboembolism with complete remission of symptoms after induced fibrinolysis, without proof that the clots were lysed. An incomplete recanalization of the vessel through partial thrombolysis probably occurred. Despite these controversial results, there is hope that fibrinolytic agents of human or non-human origin will prove most helpful to patients suffering from thromboembolism.

Nature Of The Fibrinolytic Agents

Despite the name, "fibrinolytic" agents, these substances are not specific for the lysis of fibrin. I do not know of any fibrinolytic agent of human or non-human origin which is specific for fibrin. They all attack other proteins to some degree. As was mentioned before, plasmin attacks fibrin, fibrinogen, Factor V, VIII, prothrombin and the split products of fibrinogen which exhibit further anticoagulant properties.[13, 14]

In the application of fibrinolysis for clinical purposes, after the establishment of thrombosis, it has to be emphasized that the sooner the introduction of plasmin, streptokinase, or any other fibrinolytic agent, the better the results. It has been demonstrated by experimental thrombosis, and also from pathological findings in humans, that a fresh clot is covered by endothelium within 48 hours or sooner. After the establishment of endothelium on the surface of the clot, it is very difficult for fibrinolytic drugs to penetrate it, and thus lyse the clot. Although I have observed that *in vitro* segments of old human thrombi were lysed partially within 18 hours in a strong solution of plasmin, I think if the propagation of a new clot is in process, the administration of fibrinolytic agents can have a beneficial result, even if used after 48 hours. As a rule they should be administered within 24 hours if possible.

Difficulties In The Proper Application Of Fibrinolytic Agents

One of the main problems which confronts the clinician in the administration of available fibrinolytic drugs is proper dosage. How many units of plasmin or streptokinase should we use? A standard schedule is not available which the clinician can use to induce effective fibrinolysis. The following reasons will explain the difficulties of this problem.

(1) The level of antiplasmins varies considerably in different patients, accordingly: 43,000 to 410,000 units.

(2) The antistreptokinase titer also varies considerably within a range of 40,000 to 470,000 units. This means that the dosage of plasmin or streptokinase which might be effective for one patient is inadequate for another, while excessive for a third. To induce effective fibrinolysis the level of both antiplasmins and antistreptokinase must be known. This may be one of the main reasons for the controversial results of different investigators. Some investigators use as a criterion for the therapeutic level of fibrinolysis glass clotting time after the first administration. Their tests, though useful, do not help to establish the initial dose but they are a fair gauge as to subsequent doses. Others use as a criterion for the effective dose the clot lysis time which they consider proper provided that it is lower than one hour during treatment.[15]

(3) In some preparations the amount of plasmin is known, but the amount of streptokinase is not known. It is obvious that it is extremely difficult, with these preparations, to arrange the effective dose even if the level of antiplasmins and antistreptokinase titer are known. These represent briefly the main difficulties in the proper use of fibrinolytic agents. Arbitrarily, for intravenous thrombosis 1,000 units of fibrinolysin per kg. body weight, per hour, for 4 hours is considered effective. For intra-arterial thrombosis the time required is much longer because of mechanical reasons. The proper use of streptokinase is more difficult. A large dose of streptokinase should be given at the onset, equivalent to the sum of antiplasmin and antistreptokinase units and then continued with smaller doses of 5,000 units per hour. The fibrinogen deter-

mination should be checked often since there is always danger of fibrinogenemia.[16]

Side effects: Originally a high percentage of toxic reactions were observed due to streptokinase. Today with the use of more purified streptokinase the rate is much lower. Fever, chills, hypotension, vomiting, nausea, abdominal pain and hemorrhages are the more common toxic effects. Embolization which was expected because of fragmentation of the clot was rarely observed. Another disadvantage of streptokinase, and streptokinase activated plasmin is that they are both highly antigenic, thus not permitting the readministration after appearance of antibodies. This sensitivity is not decreased even after two years. Some investigators combine fibrinolytic therapy with the use of anticoagulants. The purpose of anticoagulants is to prevent regeneration of thrombus in the affected vessel. From the theoretical view there is a logical basis for combined treatment. However, available data is not adequate for statistical analysis. In our Research Department we did find, to some degree, that large doses of heparin inhibit the fibrinolytic process *in vitro*;[17] however, moderate ones do not interfere with the effect of fibrinolysis. The experience we have had from the administration of urokinase (activated plasmin) is limited. However, it seems that urokinase as an activator is a promising one. *In vitro* studies indicate that plasmins produced by means of different activators or other techniques (chloroform, glycerol) are not equally sensitive to the inhibitors of plasma or serum. That activated by urokinase has proved more stable than plasmin produced by means of streptokinase. Other proteolytic enzymes of non-human origin (from molds or bacteria) are still in the stage of purification and experimentation in animals. One of them is Aspergillin O from Aspergillus oryza which has not yet been tried in cases of thrombosis. The second one, an enzyme from old cultures of Pseudomonas, is still under purification. To date it has not been used in humans but only in experimental thrombosis in animals; however, the results are encouraging.[18]

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Presented as a scientific program of the regular monthly meeting of the Bridgeport Medical Association, November, 1961. All papers have been reedited and brought up to date.

DISCUSSION

Dr. Nathan H. Friedman:

Now that the more formal part of this symposium has been completed, perhaps we could have a bit of fun by having the panelists ask each other some questions, but we shall first have questions from the floor.

Dr. Milton Cooper:

The only thing that I would like to ask Dr. Rosenthal about especially is what his experience has been with the thromboplastin generation test? We still encounter patients who, historically, after extractions and after operative procedures, definitely seem to be bleeders even though present tests do not define exactly what the defective factor is. Do you prepare these patients and do you set up a routine to follow them with fresh plasma?

Dr. Martin C. Rosenthal:

Well, so far as uncovering such patients, I find that the thromboplastin generation test is a good test to bring out certain physiologic factors. It is a difficult test to perform routinely in the laboratory because of its sensitivity. Perhaps many here do not agree with me with reference to the TGT test. One mixes a lot of things together and while it is claimed to have a good deal of sensitivity, I have seen errors made with the test. When we really want to find out whether an individual is a hemophiliac or not, we put them through the acid test. We call a patient with hemophilia into our laboratory, usually a severe one, and compare mixtures of fresh whole hemophilic blood with the individual in question. We also compare it with pooled normal plasma and in this way, you can uncover defects quite readily. The problem is to find a hemophiliac at such times. More recently, we have used assay procedures, using stored plasmas with specific defects as the substrate. By either method we have been able to diagnose patients that we could not uncover by other means. I would say that when patients tell us that they are repeated bleeders especially upon dental extractions or tonsillectomies, that they without question are hemophiliacs and it is not demonstrable. I do not know that I would go so far as to prepare such patients if I didn't make the diagnosis. What I would do is to put them in the hospital and start the procedure. If bleeding occurred, I would then treat them with the universal antidote, fresh whole blood. I would not know whether they were hemophiliacs but I would give them fresh whole blood or plasma. It so happens that I have one or two patients who do respond to plasma in whom all the special methods available for diagnosis have proved to no avail. I would say, do not allow the patient to start out without being prepared to handle him as a hemophiliac.

Question From The Floor:

If fresh whole blood is unavailable, would fresh frozen plasma do?

Dr. Martin C. Rosenthal:

Yes. One certainly would use fresh frozen plasma. Quite frequently we have trouble getting fresh whole blood in the city of New York. It is a rarity and it is harder to get there, I think, than it is here. Fresh frozen plasma has almost the same activity as fresh whole blood but not quite as much. Storage at minus 20° C. causes a loss of about 50 per cent in the antihemophilic globulin content in about four weeks so that it isn't quite the same potency but it is useful enough. One other point: when I say fresh whole blood, usually I refer to the freshest blood you can get. If you are in a jam and you can't get absolutely fresh blood or fresh frozen plasma, then use the freshest banked blood that you have. Today, with the blood banking systems that we have, especially with plastic bags, even at the end of a week, a significant number of bloods will have a good deal of their potency of antihemophilic globulin or labile factor still retained. Because of good refrigeration, good collection systems and good methods of preservation, we can relax the insistance on blood only a few hours old.

Dr. N. Creaturo:

I would like to thank the members of the panel for their excellent discussion. However, I would like to ask Dr. Rosenthal what the minimum procedures are that he uses at his institution for screening patients for tonsillectomy? Also having a known pseudo-hemophiliac who is not anemic, what would he do to prepare such a patient for gastric surgery?

Dr. Martin C. Rosenthal:

The first question is a very difficult one because I might answer it as a medical expert but I can't answer it as an expert lawyer. This is a problem. We do not do any screening. We at one time used to do routine bleeding times and clotting times for the ear, nose and throat department and then we decided that it was a farce. We just don't do anything now. I think in a community where all hospitals are agreed upon this, a family history, the patient's history, and a decent physical will serve in lieu of laboratory tests that mean very little.

The second question, I believe, was the preparation of a patient with pseudo-hemophilia for gastric surgery. Pseudo-hemophilia is a peculiar disease. It would be hard to historically go into the variations as to what it is considered. It was at one time thought to be a platelet abnormality. Later on, it was considered a blood vessel abnormality. Of late, it is considered to be a protein abnormality. It is now back into the clotting field, and it's a peculiar kind of protein abnormality, in that it is a protein found in fraction I in conjunction with antihemophilic globulin, but distinct from it, which has some effect upon bleeding from vessels. Furthermore, many of the patients with pseudo-hemophilia have in addition to this vascular bleeding, true hemophilia. They have an anti-hemophilic globulin lack plus the vascular defect and today are given the "terrible" term, vascular hemophilia. On theoretical grounds, if one were to give them fresh plasma, the fresh plasma would restore the antihemophilic globulin lack. It would also restore the protein that is necessary for the integrity of the blood vessel or whatever it is that is necessary to shorten the bleeding time to normal. In Sweden, the Blömbacks and Niellsen have made concentrates of this material and have been able to shorten both the clotting time and the abnormal bleeding time of such individuals. Our own experiences have been very disappointing. In general we have been able to correct with ease the hemophilic component, but we have not influenced the bleeding time and we have tried fresh plasma as well as other measures. Now, very frequently, people will have prolonged bleeding times but instead of being up to 6 minutes, it will be 8 or 10 minutes. These people in general don't really bleed. But, if you have a patient in whom, when you make a little nick in their arm and you blot and blot and you keep blotting from 40 to 50 minutes and up to 2 to 4 hours, these people are true pseudo-hemophiliacs. There is nothing that I know of that we have in this country that can control such a patient. Now I haven't told you what to do. Perhaps it would be best to send the patient over to Sweden.

Dr. J. Haskell Milstone:

I think I understood Dr. Rosenthal to say that when he treated his obstetrical problems that he interspersed the fibrinogen with whole blood. I want to second the motion for this type of therapy. I think one of the advantages one gets in addition to those he mentioned is that one has some of the inhibitory material that is going to help slow down the fibrinolytic effect, for it is present in whole blood. Now, there is another question that I would like to put to both the other members of the panel. I think it is of considerable practical importance sometimes when a patient who has a cirrhotic liver bleeds and one is not sure whether this patient is bleeding through varices or because of a bleeding defect. Sometimes the bleeding is not necessarily due to a low prothrombin either, and there have been suggestions that it may be due to something wrong with the fibrinolytic balance. I'd like to hear some comments on that.

Dr. Martin C. Rosenthal:

Cirrhotics have a very complex bleeding problem as Dr. Milstone implied. To deal with them from the hemostatic viewpoint is most difficult. They can have anything wrong with them from thrombocytopenia, to prolonged bleeding times, positive tourniquets and active fibrinolysis to almost any complication, plus the fact that they have local varices. But I want to point out one thing, that when we have worked up patients with cirrhosis, as candidates for shunt procedures for instance, we have found that most of these patients taken by ordinary criteria would be excluded from surgery. They are bad risks. You can't get a normal prothrombin time in them, you can't get a normal bleeding time. Everything that can possibly be wrong with these patients is wrong from a hemostatic viewpoint. And, discussing this problem with Dr. Hanger, he says, and I believe him, that hematologists have done a great disservice to drinkers because, he said, if it were up to the hematologist, none of his patients ever could come to an operation. The fact of the matter is that one can operate on these people and we do operate. You have to be prepared to accept some bleeding. You have to use fresh blood. Again, it pulls you through somehow, but I want to emphasis that any patient who is a cirrhotic may have many clotting abnormalities and you have to be prepared to recognize this and to think of it in such terms. I would be interested in Dr. Adamis's feelings about this.

Dr. D. Adamis:

Lately we have been examining the level of the different antiplasmin inhibitors in patients with liver cirrhosis and we have found that it is markedly increased. These patients also have an increased fibrinolytic activity. In other words there is an unbalanced situation between the fibrinolysin and the antifibrinolysin of the blood with the predominance of the former. So despite the increased level of antifibrinolysin, the patients have a tendency to bleed. Of course, other reasons contribute to these hemorrhages as mentioned by Dr. Rosenthal. Any surgical procedure in these patients is very dangerous. In three cirrhotic cases I noticed severe shock postoperatively. Their blood would not clot no matter how much fresh blood they were given, they couldn't recover and they died. I feel that it is rather risky to operate on patients with cirrhosis of the liver.

Hypercoagulability—Theory And Practice

Herbert S. Sise, M.D.

■ Physicians have long suspected that certain patients develop more extensive and repeated intravascular clots than others. For example, one person may develop phlebitis and a pulmonary embolus following an apparently innocuous leg injury, while others seem immune. Another may suffer arterial thrombosis with minimal, if any, underlying atherosclerosis, while his counterpart with extensive atherosclerosis may never have any thrombotic involvement. The observation of consecutive emboli in patients with rheumatic heart disease interspersed with long periods of freedom has led to the suspicion that there may be periods of hypercoagulability responsible for these emboli coming in "bunches." The basis on which a state of "hypercoagulability" exists is made complex by the fact that there always seems to be some causative agent such as trauma, tumor, injury, stasis, etc., so that it is very rare indeed to see an individual with completely unprovoked intravascular thrombosis. Yet, as indicated above, instances of extensive thrombosis upon little provocation continue to remind clinicians that such a state does exist. As a result, the term "hypercoagulable state" can best be defined as that state in which thrombi are prone to form abnormally and to the detriment of the organism upon provocation which usually would not lead to such extensive thrombosis. Precise knowledge as to the nature and degree of provocation and response is woefully lacking.

Clinical Conditions Suggesting A Hypercoagulable State

The association of cancer and venous thrombosis has been known for many years. Trousseau nearly 100 years ago demonstrated this association to be sufficiently important to state that the presence of phlebitis was an indication of the possible presence of visceral cancer. It has subsequently been shown that attacks of phlebitis are observed in about one-third of patients with cancer of the pancreas, the incidence rising to 50 per cent in those involving the body and tail. The phlebitis occurs predominantly in mucin producing cancers, the frequency is proportional to the grade of malignancy, the presence of jaundice is associated with a decreased incidence of attacks, and the attacks subside on removal of the cancer. There is apt to be resistance to the effects of anticoagulants, and attacks are often associated with unexplained bleeding when the prothrombin times are within the therapeutic range. The phlebitis associated with cancer usually takes the form of phlebitis migrans. The lesions are often localized in short segments of veins, recurrences and remissions in the same or other veins are frequent, and non-bacterial fibrinous (marantic) vegetations appearing on the heart valve cusps during the late stages may give rise to arterial emboli. Although it is felt that the most logical explanation for such widespread thrombosis is that the cancer itself liberates a material which promotes intravascular thrombosis, no such substance has as yet been identified. No histological changes in the blood vessels have been observed to explain any increase in the tendency for intravascular coagulation. Although cancer of the stomach, gall bladder, liver and lung, urinary bladder, ovary, rectum and uterus as well as lymphoma and leukemia are often associated with phlebitis, cancer of the body and tail of the pancreas remains as the outstanding example of this association.[1]

There is accumulating a body of indirect evidence which is pointing toward existence of a hypercoagulable state in atherosclerosis. The platelets have been found to be more adhesive than normal.[2] The turnover of platelets as indicated by their survival time following isotope tagging is faster than normal.[2] Other tests such as thromboplastin generation test,[3] and "plasma thromboplastin test"[2] and a test believed to indicate a specific substance called TGA (thromboplastin generation accelerator)[4] have all tended to indicate increased activity in patients with artherosclerosis. It seems likely that some of these results are due to activation of the initial stages of clotting. An effect similar to these observations can be seen when normal blood comes in contact with a foreign surface such as glass or certain activating agents such as celite and carboxymethyl cellulose. Here as a result of the contact, an inactive precursor (factor XII, Hageman factor) is altered to become an active accelerator of the initial stages of clotting.

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The activated factor XII then reacts with factor XI (plasma thromboplastin antecedent) to form what is known as "activation product." This does not involve an increase in the amount of any factor but rather a change from inactive to an active state.

Wright[5] describes a family with an unusually high incidence of thromboembolic disease. Nygaard & Brown[6] report five cases of essential thrombophilia with arterial and venous thrombi forming in vessels with little or no underlying vascular pathology. These conditions likewise seem to be instances where intravascular thrombosis occurs with little or no obvious provocation and strongly suggest a state of "hypercoagulability."

Following discontinuation of anticoagulants there has been reported an increase in incidence of thromboembolic episodes.[7] Whether this "rebound effect" represents a true hypercoagulable state, or merely the release from the protection of the anticoagulant allowing thrombosis to take place in diseased vessels, has not been clear. In the experience of this laboratory, the early recurrences were noted almost exclusively in those in whom anticoagulant treatment had been stopped because of bleeding. We have postulated some factor related to bleeding, possibly anticoagulant overdose or possibly something related to blood in the tissues itself as being important in the mechanism of this rebound thrombosis.[8]

Other conditions in which thrombosis is apt to occur may be associated with what might be considered a strong provocation. These conditions, of course, include injuries, myocardial infarction, congestive heart failure, pregnancy, postpartum state, postoperative state, trauma and air-raid shelter thrombosis. In these instances either unusual stasis or tissue damage are obviously contributory. On the other hand, it is not clear why some individuals may develop extensive thrombosis, while others happily seem to be immune.

Diagnosis Of Hypercoagulable State

Clinicians have long searched for ways of identifying those who would be more susceptible to developing thrombosis. It was natural at first to use available tests for this purpose and attempts centered around equating a short clotting time by some test with a state of hypercoagulability. For instance, the shortening of a prothrombin time has been considered to be evidence of a hypercoagulable state. Examination of the reports drawing such conclusions usually indicates that the prothrombin time was done by the Link-Shapiro method where the plasma is diluted with saline. This procedure dilutes the fibrinogen so much that the test becomes sensitive to levels in fibrinogen. Following tissue damage such as myocardial infarction, or tissue necrosis due to trauma, the fibrinogen level may become considerably elevated. This results in a shortening of the diluted prothrombin time. If the prothrombin time is done, either undiluted or by diluting with barium sulphate adsorbed plasma so that the fibrinogen concentration does not become critically lowered, the prothrombin time is found to be unchanged or, if anything, prolonged. Original hopes that the shorter prothrombin time would indicate hypercoagulability have been unrewarding.

The shortening of the clotting time of whole blood in either glass or silicone tubes may possibly lead to erroneous conclusions. Such shortening may be seen with the ingestion of a fatty meal, exercise epinephrine or steroids. This result has lead to the implication that after a fatty meal there is a state of "hypercoagulability." Yet, experimental evidence has never substantiated this conclusion in humans.

Heparin retarded clotting times and the intravenous heparin tolerance test results have shown certain changes after myocardial infarction, operation or thromboembolic events. They have been regarded as indicating an overall state of hyper- or hypocoagulability. The specific change in the coagulation system responsible for these alterations has never been identified. Furthermore, it is known that this system is very sensitive to changes in the level of heparin co-factor. Heparin co-factor appears to be identical with antithrombin. Antithrombin is noted to vary widely in certain disease states, particularly when the pancreas is involved. This variation should lead to a critical attitude toward interpretation of heparin retarded clotting times.

It would appear risky then to define a "hypercoagulable state" merely by finding a shorter than normal clotting time on a particular test.

Elevated levels of coagulation factors have been proposed as a cause of hypercoagulability. The association has been infrequent and unconvincing. In fact, it would seem more reasonable if clotting was going on more rapidly than normal in the body that perhaps some of the clotting factors would become depleted.

Indeed it seems reasonable to examine some states in which coagulation is known to be going on more rapidly than normal in order to observe what tests might be useful in detecting a hypercoagulable state. There are a number of such interesting conditions. In abruptio placenta large retroplacental clots form and thromboplastin is probably liberated into the blood stream. There seems to be very little doubt that coagulation is going on so fast in this condition that the subject becomes defibrinated, suffers from reduction in platelets and actually develops a bleeding disorder as a result. A similar state may happen in ammiotic fluid embolism. It would appear that during extracorporeal pumping of blood for open-heart surgery there is tendency for the blood to clot in the extracorporeal machinery. This, of course, can largely be prevented by the use of heparin. Some coagulation seems to take place, however, because there still may be a fall in certain coagulation factors, particularly platelets. Penick and McLendon[9] point out many instances of paradoxical "thrombosing bleeders." They postulate that disemminated thrombosis may lead to depletion of clotting factors and ensuing bleeding.

Brinkhous and Penick[10] have created experimental conditions in animals which substantiate this hypothesis by inducing local tissue injury in dogs through freezing a controlled area of skin with liquid nitrogen. They observed a decrease in the circulating levels of platelets and factor VIII (antihemophilic factor). In a series of well conceived experiments they could show very nicely that circulating thromboplastin causes depletion of factor VIII first by utilization in the coagulation induced by the thromboplastin, and secondly, through its destruction by small quantities of thrombin which were evolved in the process of the induced intravascular coagulation. They imply that a lowering of the level of factor VIII would be associated with increased intravascular coagulation.

As a corollary to these observations, if intravascular coagulation is slowed, one might expect the level of factor VIII to become elevated. Indeed this has been found to be so. In patients who have thrombocytopenia, we observed increases in the level of factor VIII up to 400 per cent of normal.[11] This rise may also be seen following anticoagulants either of the coumarin variety or after heparin. A similar rise in the level of factor VIII has been observed after exercise, epinephrine, operation and possibly some steroid drugs, but what relation this finding may have to coagulability is not known.[12] Finally, the Bantu of South Africa is observed to have higher levels of factor VIII than normal white men.[13] This tribe of natives is known to have a nutritional deficiency often resulting in a nutritional liver disorder. They rarely have coronary artery disease or phlebitis.[14]

Paradoxical as it first seems, a high level of factor VIII may indicate a hypocoagulable state and a low level may be associated with a hypercoagulable state. Promising as this field appears to be in opening up new avenues of approach to the problems of intravascular coagulation, there is still no application available to the clinician for the laboratory detection of clinical states of hypercoagulability.

The only way that the hypercoagulable state becomes recognized at present is through the presence of a thromboembolic condition. Too often this may be too late. For example, it is estimated that over half of fatal pulmonary emboli fail to be preceded by any clinical warning.[15,16,17] Lacking any clinical test which can anticipate a pulmonary embolus, clinicians have learned to realize the importance of the circumstantial factors. A hemoptysis happening in an ambulatory otherwise asymptomatic individual, brings to mind the diagnosis of tuberculosis, bronchiectasis or tumor, but the same happening about seven days after a cholecystectomy immediately focuses attention on the likelihood of a pulmonary embolus. In a patient bedridden with a fractured hip, any untoward event immediately raises the suspicion of a pulmonary embolus. Sevitt and Gallagher[18] at the Birmingham Accident Hospital in England have made the sobering observation that thrombosis often extensive in the lower venous tree is found in at least 65 per cent of injured patients who come to autopsy. Pulmonary emboli were found in 20 per cent of all necropsies, and in about three-quarters they were the major cause of death.

In a similar manner, it may be considered that atrial fibrillation with tight mitral stenosis is a potential source of embolus given the proper set of circumstances. The factors responsible for development of a thrombus in the left atrium can easily come in to play. There is already stasis. The distended atrial wall may be traumatized sufficiently to contribute the factor of intimal surface injury. Finally, minor remote trauma, infection, or other unknown circumstances may supply the factor of a systemic hypercoagulability which will precipitate thrombus formation.

Other hypercoaguable states may be presumed to exist in atherosclerosis, cancer, leukemia, postpartum state and in other hematologic disorders. The decision as to when the circumstances justify active prophylaxis have not been clearly worked out in most instances. In special groups of patients with myocardial infarction, angina and cerebral thrombosis, studies have indicated some order of success in the use of anticoagulants prophylactically.

A plea is made at this juncture to recognize the use of anticoagulants as a tool for the study of the part played by thrombosis in coronary artery disease. For example, in our laboratory and elsewhere, it is noted that the prevention of recurrences by long-term anticoagulation in myocardial infarction is more striking than the prevention of death.[19,20] This immediately leads to the appreciation that death in coronary artery disease is most often not a thrombotic event (otherwise it would have been prevented), while recurrent infarction most often is. Reference is made to an autopsy study of the cause of death in coronary sclerosis by Spiekerman, et al.[21] where sudden unexplained death and congestive failure, both non-thrombotic conditions, accounted for over half of the deaths. It is difficult to conceive that anticoagulation could be effective in preventing such non-thrombotic events.

Pathophysiology Of Hypercoagulability

Information in regard to the mechanisms involved in hypercoagulability has been heretofore limited due to the lack of an experimental tool. Attempts originally were made by injecting thromboplastic substances intravenously. This procedure led to diffuse thrombosis of the pulmonary vessels and death of the animal. Little could be learned concerning clinical applications. Thrombi produced by vessel wall injury, while aiding in studying the early stages of clot formation, was of no help in elucidating the systemic hypercoagulable state. Extensive studies of thrombosis induced by changes in the electrical potential across the vessel wall have likewise stimulated interest in the mechanism of the vascular factor but have not contributed to the study of the circulating hypercoagulable factor.

An experimental method of producing thrombosis by intravenous injection of serum, however, deserves attention since it more nearly simulates human counterparts. Wessler[22] has made extensive observations which are herein summarized. The technique consists of carefully isolating a segment of the jugular vein of the experimental animal and applying non-traumatic clamps to both ends of the segment. If this is carefully done the blood will stay liquid for several hours within the segment of vein. If serum is injected into the blood stream at a site remote from the isolated vein, a clot will form in the isolated segment in a matter of a few minutes. The clot is not adherent to the wall and the wall of the vein shows no sign of any inflammatory process. No clot forms unless the blood flow in the vein is stopped by clamping off the segment of vein. The factor in serum responsible for this systemic hypercoagulable state has been given the name of serum thrombosis accelerator (STA). The evolution of STA has been shown to be dependent on factor IX (Christmas factor or PTC), factor XI (PTA) and factor XII (Hageman factor) and activation by glass or other agents. STA is not a separate clotting factor but a product of interaction of the aforementioned factors. It is removed by the liver in one circulation. Results similar to the injection of serum can be obtained by the intravenous injection of materials which have potent surface activating properties such as celite or of plasma activated by carboxymethyl cellulose or celite.[23] This experiment illustrates that some provocative factor (in this case stasis) is necessary as well as the systemic hypercoagulable state to result in local thrombosis.

It would not be a great stretch of the imagination to consider that such surface activation could take place in humans. For instance, in atherosclerosis activation could take place by the atherosclerotic plaques. Possibly cancers could act in a similar pattern. On the other hand, no such mechanism has been proven in man. It will be most difficult, moreover, to design an experiment which could detect this type of mechanism working with the present tools available for such study.

Still other mechanisms may be operable in the systemic hypercoagulable state. If a small dose of serum is given, one which is just able to produce a small thrombus on the average, a different response may be observed from animal to animal. A large clot may form in one and none at all in another. In an experiment designed to be a model of the patient who has had anticoagulation stopped because of hemorrhage (post hemorrhagic rebound) animals were similarly treated with anticoagulants, hemorrhage induced by a surgical incision and anticoagulation terminated abruptly with Vitamin K_1. Four to five days later these animals responded to critically small doses of serum with more extensive thrombosis than untreated animals.[24] This experiment suggested another mechanism of hypercoagulability than the STA system.

Another systemic hypercoagulable state is suggested in an experiment where large doses of long-chain saturated fatty acids and a fibrinolysis antagonist are fed to rats.[25] Observation of the heart chambers in these animals has disclosed extensive thromboses. Speculation on the relationship of the dietary background of atherosclerosis is tempting. The possibility of endocardial damage, however, remains to be excluded.

Finally, the systemic and local administration of antiheparin compounds such as protamine, toluidine and hexadimethrine has been found to render local thrombosis following vessel wall injury earlier.[26] Just how physiologically possible this is in the human is doubtful but indicates a chance that chemical interference with the heparin contained in mast cells which are found in the intima may play a role in producing a local chemical vascular change and what we suppose is a systemic disorder may indeed be localized to the vessel wall.

Clinical Application

To return to the clinical applications of these considerations of the hypercoagulable state, we find certain axiomatic guidelines to the management of problems involving thrombosis.

1. Phlebitis particularly if migratory and superficial in an otherwise healthy young individual, or pulmonary embolus in a setting where explanation is lacking, should lead to a suspicion of a visceral cancer particularly of the body or tail of the pancreas.

2. Routine prevention of thrombosis and embolus should be considered in certain high-risk conditions. (a) Cancer of the pancreas, (b) injuries, particularly with fractures of the hip requiring three days bed rest or more, (c) post operation, (d) post partum, (e) mitral stenosis, (f) congestive heart failure, (g) myocardial infarction, (h) gangrene, (i) burns, (j) postanticoagulant hemorrhage.

3. If embolism or thrombosis has already taken place, more forceful prevention must be considered.

4. There are five possible methods of prevention of thrombosis and embolism.

   a. Reduction of stasis in the legs by stockings, ambulation and leg exercise.

   b. Administration of anticoagulants.

   c. Surgical measures to either interrupt routes of embolization (such as vein ligation) or reduce stasis (such as mitral valve operation in mitral stenosis).

   d. Diet? (a remote possibility).

   e. Exercise? through evolution of changes in the natural pro- and anticoagulants.

5. Intravenous infusion of serum should be avoided because of its possible thrombogenic effect. Since glass activation of plasma can evolve STA, plastic bag blood is theoretically preferable to aged bank blood in glass containers.

Following trauma such as leg fractures particularly of the hip where long periods of immobilization are necessary, surgical ligation of veins was first practiced but this procedure has currently lost favor. The use of anticoagulants prophylactically has been championed by Sevitt[17] with some very convincing clinical and postmortem material to support his claim. In a controlled series of patients with and without prophylactic anticoagulant treatment, he showed a remarkable degree of reduction of leg vein thrombosis, deaths from pulmonary emboli, as well as clinical and postmortem evidence of pulmonary embolus. He recommends routine anticoagulant treatment in all injured patients over forty years of age who will be required to remain in bed more than three days. Routine treatment at this point could hardly be uniformly recommended, but individual consideration should certainly be given to treating some patients.

It is possible to reduce stasis in the legs with routine use of elastic stockings in postoperative and postpartum patients and in certain medical patients, particularly those with congestive failure. Early ambulation and the encouragement of leg exercises are simple practical procedures which certainly are not harmful and may be truly beneficial.

Reduction of the incidence of pulmonary emboli has been reported by the use of elastic stockings.[26] The routine use of small doses of dicoumarol has been proposed and in one instance a report,[27] although lacking strict control, points to the necessity of more detailed investigation of the possibility that homeopathic doses may have some effect in suppressing postoperative thrombosis and pulmonary embolism. Routine vein ligation has been used only sporadically and its effectiveness questioned.[15]

Following myocardial infarction, the principle agent used is anticoagulation. Reduction of stasis is impossible except in the legs by elastic stockings and ligation is obviously unavailable in the prevention of the mural thrombus and the arterial embolus. While it is overwhelmingly evident that reduction in thromboembolic complications may be so achieved, the reduction in mortality rate is disappointingly little as noted above. The possibility that diet and exercise may have some prophylactic value here should not be ruled out.

In cancers, the most nearly ideal opportunity for cure of a "hypercoagulable state" exists in removal of the cancer. Unfortunately, the number of times that such an opportunity leads to cure is limited particularly in cancer of the pancreas where metastasis has nearly always occurred by the time the primary site has been rocognized. The use of the routine prophylactic procedures, stockings, anticoagulants, or ligation, is most often limited by the clinical situation.

The presence of an embolus or arterial thrombosis is often the first sign of thromboembolic disease in many instances. Here further prevention can be achieved only with anticoagulation because of the unavailability of the arterial lesion to reduction of statis or surgical ligation. One exception is mitral stenosis where embolization axiomatically indicates the presence of a tight mitral stenosis, and until proved otherwise, operation should be performed provided appropriate studies justify the procedure.

The hypercoagulable state that follows interruption of anticoagulation for hemorrhage deserves some special attention because it requires a rather bold approach. Since there is a one out of three chance of thrombo embolism or death,[8] the prevention of "rebound" thrombosis is mandatory.

Because of the nature of the disorder under treatment, and the inability to predict when thrombosis may happen, prevention of stasis and surgical procedures are inappropriate. This means that anticoagulation, the very source of the catastrophe, is the only available measure. Most clinicians are unwilling to run the risk of bleeding again only to be sorry when a rebound thrombosis happens. We have recommended the following procedure in patients whose anticoagulant dose has been established.

1. Give Vitamin K_1 10 to 50 mg. by mouth, intramuscularly or intravenously depending on the severity of bleeding and condition of the patient. While the intravenous route should be avoided due to reactions, we have noted one patient who was unresponsive save by this route.
2. Continue the coumarin anticoagulant at a dose 25 per cent lower than that which resulted in the hemorrhagic level (assuming enough time has passed to clearly establish this dose).
3. Continue the coumarin at least 4 weeks if possible before stopping if it is decided that further long-term treatment would be too hazardous.

The result is that the prothrombin time returns to normal in a matter of 6 to 12 hours, and bleeding ceases. The prothrombin time then returns to a therapeutic level in a matter of 5 to 6 days and at the lower dosage does not give rise to hemorrhagic levels.

In conclusion, clinicians must always be alert for the insidious problem of thrombosis. Recognition of a hypercoagulable state is impossible except in retrospect. Certain high-risk states, however, can be assumed to be associated with a high rate of thromboembolism and certain preventive measures (reduction of stasis, prophylactic anticoagulation, surgical interruption of pathways of emboli, diet and exercise) may be appropriately selected to fit the condition. The problem may be thought of as centered about two etiologic factors—the provocative factor (stasis, vessel wall injury) and the systemic hypercoagulability factor. "Abnormal" thrombosis may rarely be seen with what seems to be only hypercoagulability and no provocation. In most instances it would seem that both factors are required before pathological thrombosis will develop. This association often allows more than one preventive measure, such as the combination of anticoagulation and measures to reduce stasis for example, to be used in any given case.

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Atherosclerotic Coronary Heart Disease

The Major Challenge To Contemporary Public Health And Preventive Medicine

Jeremiah Stamler, M.D.

■ This paper attempts to evaluate four major questions confronting contemporary American medicine: (1) The evolution of the public health situation in the United States in the twentieth century; (2) the scope and nature of the chronic disease problem in this country today; (3) the research advances indicating the possibility of a successful preventive advance against the major chronic disease, atherosclerotic coronary heart disease; and (4) the current status of the research and developmental efforts to achieve effective primary and secondary prevention of this disease, and the responsibilities of medicine and public health in these efforts.

The Evolution Of The U. S. Public Health Situation

As is well known, the public health situation has changed drastically in this country in the last sixty years, with the noninfectious chronic diseases replacing the acute infectious diseases as the cardinal and most pressing health problems. It is valuable, by way of introduction, briefly to review and summarize what has happened. First and foremost is the very significant fact that in the twentieth century, approximately 25 years has been added to the life span of new-born American infants (Table I). It has gone up from about 45 years in 1900 as an average figure, to almost 70 years today. These are approximate overall averages. It is worthwhile to examine the detailed data with respect to the major sex-race groups, because this helps to pinpoint the chronic disease problems. Thus, the best life expectancy today is that of a new-born white female baby—73.9 years. The white male baby has a life expectancy of 67.3, a sex differential of almost six years—to be discussed later, since it merits detailed attention. Negro new-born infants, male or female, are about six or seven years worse off in their life expectancy today, compared to corresponding white babies of like sex.

The sex differential in life expectancy has increased significantly in the twentieth century, mounting continuously to attain today's big differential of six years—for both whites and Negroes. The race differential has narrowed. In 1900, the race differential in life expectancy of new-born infants was over fifteen years. It has now been narrowed to about six, almost certainly due to improved social conditions for Negroes, including better preventive medicine and medical care. It is sound to infer that this differential has to do with social conditions and has little or nothing to do with inherent, genetic racial characteristics.

This great increase in life expectancy in the twentieth century is overwhelmingly due to achievements with respect to infectious diseases—chiefly the infectious diseases of infancy and childhood. A few additional statistics serve to drive this point home. In 1900, of a thousand new-born white infants, about 200 or 250 were destined to die before their fifteenth birthday—200 or 250 (Table II)! The corresponding figures for Negroes were about 500 or 550 dead by their fifteenth birthday—500-550 per thousand! This, of course, was due to the tremendous toll exacted by the infectious diseases, particularly during the first year of life.

Contemporary conditions in this area are a far cry from the situation prevailing early in the 1900s. When one wished at the turn of the century to rear three or four children to adulthood, one had several babies because it was "par for the course"—

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TABLE I

LIFE EXPECTANCY AT SPECIFIED AGES FOR THE U. S. POPULATION BY SEX AND COLOR, 1900-59

	WHITE MALE			WHITE FEMALE			NONWHITE MALE			NONWHITE FEMALE		
YEARS	AT BIRTH	AGE 40	AGE 60	AT BIRTH	AGE 40	AGE 60	AT BIRTH	AGE 40	AGE 60	AT BIRTH	AGE 40	AGE 60
1900-02	48.2	27.7	14.4	51.1	29.2	15.2	32.5	23.1	12.6	35.0	24.4	13.6
1909-11	50.2	27.4	14.0	53.6	29.3	14.9	34.0	21.6	11.7	37.7	23.3	12.8
1919-21	56.3	29.9	15.2	58.5	30.9	15.9	47.1	26.5	14.7	46.9	25.6	14.7
1929-31	59.1	29.2	14.7	62.7	31.5	16.0	47.6	23.4	13.2	49.5	24.3	14.2
1939-41	62.8	30.0	15.0	67.3	33.2	17.0	52.3	25.2	14.4	55.5	27.3	16.1
1949-51	66.3	31.2	15.8	72.0	35.6	18.6	58.9	27.3	14.9	62.7	29.8	17.0
1959	67.3	31.5	15.8	73.9	36.9	19.4	60.9	27.3	14.9	66.2	32.1	17.8
Increase (Per Cent)												
1900-02 to 1959	39.6	13.7	9.7	44.6	26.4	27.6	85.5	20.3	15.1	86.3	28.3	27.9
Increase (Per Cent)												
1919-21 to 1959	19.5	5.4	3.9	26.3	19.4	22.0	28.0	4.9	1.4	39.0	22.3	18.4
Increase (Per Cent)												
1939-41 to 1949-51	5:6	4.0	5.3	7.0	7.2	9.4	12.6	8.3	3.5	13.0	9.2	5.6
Increase (Per Cent)												
1949-51 to 1959	1.5	1.0	0.0	2.6	3.7	4.3	3.4	3.7	0.0	5.6	7.7	4.7

part of the natural sequence of events—for two or three to die in infancy or childhood, usually from infectious diseases. Today, of a thousand new-born white infants only 30 or 40 are destined to die before their 15th birthday; for Negroes, the figure is about 60 or 70—a tremendous decline in a few decades. Mortality in the first 15 years of life, in the first five years, in the first year has been cut tremendously. The reduction is in the order of 80% to 95%. It is this phenomenal decrease in mortality in infancy and childhood—due to the conquest of infectious diseases, to improvement in the standard of living, improved nutrition, improved sanitation, improved medical care and mass immunization—that largely accounts for the overall increase in the life expectancy.

If the aim is to see the whole picture, then it must be further stressed that this achievement has been confined to the economically developed countries. By and large it is far from achieved for a majority of mankind, living in the economically underdeveloped nations of Asia, Africa and Latin America (Table III). (These statistics lie behind our daily headlines reporting political unrest and social ferment in these lands.)

Now, to the nub of present-day problems: When one poses the additional question, what is the life expectancy today of a person age 40, compared with a person age 40 in 1900, then one finds that the improvement in life expectancy for persons of this age has been discouragingly slim—particularly for the males, most particularly for the white males (Table I). For the ladies, almost eight years have been added to life expectancy at age 40 compared to 1900. For the men, only four years have been added. Progress has really been slight in this area. Adult males cannot expect to live much longer today than their counterparts could in 1900.

The reasons for this are readily apparent—and directly related to the central theme of this paper. That is, while tremendous progress has been made in this century against the infectious diseases and against the forms of malnutrition represented by under-nutrition (e.g. scurvy, pellagra, beriberi, rickets), significant progress has not yet been made against the major chronic diseases which shorten the life span and produce large scale and premature chronic disability, making life burdensome in middle-age for all too many. The major challenge today is to move forward on this front. In the twentieth

TABLE II

PER CENT OF INDIVIDUALS DYING IN INFANCY AND CHILDHOOD, BY SEX AND COLOR—UNITED STATES, 1901 AND 1959

	ALL RACES, BOTH SEXES			WHITE MALE			WHITE FEMALE			NONWHITE MALE			NONWHITE FEMALE		
YEAR	< 1*	1-4*	5-14*	< 1	1-4	5-14	< 1	1-4	5-14	< 1	1-4	5-14	< 1	1-4	5-14
1901	14.1	6.8	3.5	15.3	7.0	3.6	12.3	6.4	3.3	33.3	14.4	7.2	28.7	13.5	7.5
1959	2.9	0.4	0.5	2.9	0.4	0.5	2.2	0.3	0.3	5.6	0.8	0.7	4.5	0.7	0.5
Decline (Per Cent)															
1901-59	79.4	94.1	85.7	81.0	94.3	86.1	82.1	95.3	90.9	83.2	94.4	90.3	84.7	94.8	93.3

* Age period.

TABLE III

LIFE EXPECTANCY IN THE ECONOMICALLY DEVELOPING COUNTRIES

COUNTRY	YEAR	EXPECTATION OF LIFE AT BIRTH	
Africa			
Central African Republic	1959	35	
Congo (Leopoldville)	1950-52	38*	40△
Ghana	1949	38	
Guinea	1954-55	31	
Ivory Coast	1956-58	35	
Mauritius	1951-53	50	52
No. Rhodesia (Indigenous Pop'l)	1950	37	
So. Rhodesia (Indigenous Pop'l)	1953-55	48	49
Senegal	1957	37	
Zanzibar	1958	43	
Pemba	1958	40	
South America			
Argentina	1947	57	61
Brazil	1940-50	39	46
British Guiana	1945-47	49	52
Chile	1952	50	54
Asia			
Cambodia	1958-59	44	43
China (Taiwan)	1959-60	61	66
Fed. of Malaya	1956-58	56	58
India	1941-50	32	32
Thailand	1947-48	49	52

* Male △ Female

century, medicine and public health have stormed the fortresses and breached the ramparts of two great killers—acute infection and under-nutrition—the two scourages of plague and starvation stalking and devastating mankind for countless centuries. However, a forbidding barricade still lies astride the way to the high road of health and longevity in maturity. Hence for public health and medicine there are indeed "worlds to conquer." For no major additional advances in life expectancy are possible in the United States in the decades ahead unless significant progress is made first and foremost against the chronic diseases that today produce so much morbidity and mortality—not only among the elderly, but among the middle-aged population as well.

In contrast to the advances made against infectious diseases and malnutrition, the chronic diseases, which also existed in 1900, persist today largely unabated. Moreover, they have emerged as much more important problems both relatively and absolutely. They have emerged relatively, because the problems of infectious disease and under-nutrition have been more or less mastered and have therefore diminished markedly in their impact.

Dr. Paul Dudley White, in a talk before the American Society for the Study of Arteriosclerosis a few years ago, vividly described the situation prevailing when he was a young physician early in this century. At that time the problem was, can hospital beds be made available fast enough to take care of the cases of typhoid fever. This is indeed a far cry from the present situation.

Incidentally, the fact that that *was* the problem is a wonderful illustration of a truth that needs to be driven home continually to citizens and statesmen, to the body politic in general, to responsible people in health and medicine. It is a truth pregnant with meaning in relation to the chronic diseases and our big problems today—namely that it is almost always much cheaper to bring about preventive medicine for the tens of millions than it is to provide therapeutic medicine for serious frank illness among tens of thousands. This thesis is presented in this crass way—in hard cash terms, so to speak—because an appeal to humanitarianism, to the welfare of people is unfortunately not enough. Proposals for the distribution of the national income and the share of it assigned overall to health services must be justified and defended dollarwise. It is a very important aspect of that justification, that—as with the infectious diseases, so with the chronic diseases—effective primary and secondary prevention are not only useful in that they bring well-being to people. Their costs—even when the measures reach out to serve large populations—are often less than would have otherwise been incurred for the care of severe illness. In other words, the end result of the "big" preventive programs often is an overall saving of money. This is a very important point.

Be that as it may, a relative change in the situation has certainly occurred, namely the chronic diseases have come to the fore because other diseases have been pushed into the background. Here it is necessary to stress, in all conscience, that what has been pushed into the background will remain in the background only as long as vigilance is maintained with respect to the infectious diseases, nutrition, etc. And as the world shrinks in size and the population increases, the problem of vigilance against the infectious diseases becomes more complex, not less complex. The so-called old public health approaches are here to stay!

The Scope And Nature Of The U. S. Chronic Disease Problem Today

It is not only relatively, however, that the chronic diseases have come to the fore. They have come to the fore in two other respects. First of all, since many people have been kept alive who would previously have died in childhood, the adult population

Table IV
U. S. Population, 1900-1970, by Age

Year	All Ages	45-64 Years	65 and + Years
1900+	76,094,000	10,466,000	3,100,000
1950+	151,683,000	30,837,000	12,287,000
1960△	180,677,000	36,208,000	16,658,000
	Series II*:		
1970△	214,222,000		
	Series III*:		
	208,931,000	42,265,000	20,035,000
1900 → 1960			
Per Cent Increase	137.4%	246.0%	437.4%

+ Series A 22-33, Estimated Population, by Sex, Color, and Age. 1900-1957. *p. 8, Historical Statistics of the United States.*

△ Table No. III, Total Population, by Age and Sex: 1960 and Projections to 1970. *p. 6, Statistical Abstract of the United States, 1962.*

* Two different assumptions on fertility in period 1965-1970.

at risk with respect to the chronic diseases has been increased markedly. While the population of the United States as a whole has increased about 140% in the twentieth century, the population 45 to 64 has increased 250% (Table IV), And, the population 65 and over has undergone an even greater increase. Therefore a disproportionate increase has occurred in the number of people reaching the decades of life in which the chronic diseases are common. The result has been a gross increase in the absolute number of people with chronic diseases. This, it should be emphasized, is irrespective of any increase in age specific rates. It merely results from the fact that there are more people at risk.

But even this is not the whole story. There is good reason to believe (despite all the limitations in time trend statistics) that an absolute increase has occurred in the age specific rates of certain diseases. Thus, for the key cardiovascular-renal grouping as a whole—a broad grouping of many diseases, but principally atherosclerotic and hypertensive diseases—the data indicate that from 1920 to about 1940 mortality rates for middle-aged white males rose significantly (Tables V-VIII). In the late 1940s and early 1950s these rates plateaued and then began to go down slightly.

There is considerable reason to believe that in the twentieth century the middle-age-specific mortality rates for atherosclerotic coronary heart disease

Table V
Age Adjusted Death Rates, All Causes, Cardiovascular-Renal and Non-Cardiovascular-Renal Diseases U. S. Population by Sex and Color, 1920-1959*

		Death Rate Per 100,000 Population				
Causes	Year	Both Sexes, All Races	White Male	White Female	Non-white Male	Non-white Female
All Causes	1920	1424	1421	1314	2042	2098
	1930	1246	1276	1058	2100	1921
	1940	1076	1155	879	1764	1505
	1950	842	963	645	1358	1096
	1959	770	925	566	1258	925
Cardiovascular-Renal Diseases	1920	471	476	449	567	618
	1930	491	509	429	752	729
	1940	486	535	403	691	647
	1950	440	514	339	634	571
	1959	408	500	301	603	495
Non-Cardiovascular-Renal Diseases	1920	953	945	865	1475	1480
	1930	755	767	629	1348	1192
	1940	590	620	476	1073	858
	1950	402	449	309	724	525
	1959	362	425	265	655	430
Per Cent Change, All Causes	1920-1959	–46.0%	–34.9%	–56.9%	–38.4%	–55.9%
	1940-1950	–21.7%	–16.6%	–26.6%	–23.0%	–27.2%
	1950-1959	– 8.6%	– 3.9%	–12.2%	– 7.4%	–15.6%
Per Cent Change, CVR Diseases	1920-1959	–13.4%	+ 5.4%	–33.0%	+ 6.3%	–19.9%
	1940-1950	– 9.5%	– 3.9%	–15.9%	– 8.2%	–11.7%
	1950-1959	– 7.3%	– 2.7%	–11.2%	– 4.9%	–13.3%
Per Cent Change, Non-CVR Diseases	1920-1959	–62.0%	–55.0%	–69.4%	–55.6%	–70.9%
	1940-1950	–31.9%	–27.6%	–35.1%	–32.5%	–38.8%
	1950-1959	–10.0%	– 5.3%	–14.2%	– 9.5%	–18.1%

* The age-adjusted rates were computed by the direct method, using the total population as enumerated in 1940 as the standard.

in white males rose substantially—and either they are continuing to rise slightly or have plateaued recently (Table VIII). There is no evidence yet of a downturn in the coronary heart disease mortality rate among males nationally.

In noting this increase in certain diseases, one cannot fail to emphasize the catastrophic increase in the occurrence of certain cancers, particularly carcinoma of the lung. For many of the age-sex-race specific groups, the mortality rates in middle age due to this carcinoma have almost doubled from 1950 to 1960. Certainly this is not an artefact resulting from better diagnosis, but a true increase—attributable mostly to the impact of twentieth century cigarette smoking habits.

There is also reason to believe that an increase has occurred in incidence and mortality rates (including premature mortality rates) from chronic bronchopulmonary disease, i.e. asthma, emphysema, bronchiectasis, chronic bronchitis. These diseases—related to air pollution and smoking, particularly cigarette smoking with inhaling—are also on the increase in an absolute sense. They are already prime problems in Great Britain. While the American situation is not yet nearly as serious as Britain's, it is indeed serious enough to warrant a warning note and a call for preventive approaches, before another chronic illness problem mounts to major proportions.

Up until the last few sections, the chronic diseases have been discussed in general, as a broad group, without indicating specifics or defining terms. It is essential to get down to delineating and defining specific disease entities if the objective is development and application of preventive approaches. The assignment of specific diseases to the chronic disease group is, of course, within limits an arbitrary matter. Thus a disease like tuberculosis can manifest markedly chronicity, as is well known, but through custom it is not included among the chronic diseases. The major chronic diseases are:

(a) Certain diseases of the cardiovarcular system, first and foremost among these, hypertensive disease and atherosclerotic disease, also (far less significant nowadays) rheumatic heart disease;

(b) diabetes mellitus, of key importance today because of the added risk it gives of sickness, disability and death from cardiovascular diseases, hypertensive, atherosclerotic, arteriolosclerotic;

Table VI

Death Rates, All Causes, Cardiovascular-Renal and Non-cardiovascular-Renal Diseases, U. S. Population Age 45-54 by Sex and Color, 1920-1959

Causes	Year	Death Rate Per 100,000 Population				
		Both Sexes, All Races	White Male	White Female	Non-white Male	Non-white Female
All Causes	1920	1219	1198	1087	2009	2335
	1930	1218	1231	925	2633	2518
	1940	1060	1139	747	2453	2109
	1950	854	984	546	1857	1555
	1959	733	909	445	1511	1098
Cardiovascular-Renal Diseases	1920	387	350	359	707	923
	1930	444	417	325	1152	1201
	1940	439	480	278	1072	1058
	1950	412	508	217	903	862
	1959	341	472	150	735	573
Non-Cardiovascular-Renal Diseases	1920	832	848	728	1302	1412
	1930	774	814	600	1481	1317
	1940	621	659	469	1381	1051
	1950	442	476	329	954	693
	1959	392	437	295	776	525
Per Cent Change, All Causes	1920-1959	−39.9%	−24.1%	−59.1%	−24.8%	−53.0%
	1940-1950	−19.4%	−13.6%	−26.9%	−24.3%	−26.3%
	1950-1959	− 8.5%	− 7.6%	−18.5%	−18.6%	−29.4%
Per Cent Change, CVR Diseases	1920-1959	−11.9%	+34.9%	−58.2%	+ 4.0%	−37.9%
	1940-1950	− 6.2%	+ 5.8%	−21.9%	−15.8%	−18.5%
	1950-1959	−17.2%	− 7.1%	−30.9%	−18.6%	−33.5%
Per Cent Change, Non-CVR Diseases	1920-1959	−52.9%	−48.5%	−59.5%	−40.4%	−62.8%
	1940-1950	−28.8%	−27.8%	−29.8%	−30.9%	−34.1%
	1950-1959	−11.3%	− 8.2%	−10.3%	−18.7%	−24.2%

(c) chronic urinary tract infection, apparently a major problem, especially in women;

(d) chronic bronchopulmonary disease, involving primarily the lungs, but eventually also the heart, in chronic cor pulmonale or pulmonary heart disease;

(e) the neoplastic diseases;

(f) arthritis and rheumatism, another major grouping for which public health has little or no preventive approach to date;

(g) the mental illnesses, classified by some, but not others, with the chronic diseases;

(h) finally, very properly included with the chronic diseases, to which it contributes most significantly and deplorably, a major form of nutritional disease today—obesity, chronic malnutrition in the form of overnutrition.

Among these chronic diseases, the cardiovascular entities—particularly hypertensive and atherosclerotic diseases—are far and away the chief producers of morbidity, disability and mortality both in the middle-aged and elderly strata of the U. S. population today. One disease—atherosclerotic coronary heart disease—alone accounts for one-third or more of all deaths in white males age 45-54, and exacts a high toll in all the other sex-race groups as well (Table VIII).

The validity of this conclusion was once again verified by the data collected in an important survey recently completed by the Chicago Association of Commerce and Industry in cooperation with the Chicago Heart Association. This study demonstrated that in 1961 diseases of the heart and blood vessels were responsible for an absolute majority of deaths among 312,229 employees of 18 major Chicago companies. Cardiovascular diseases killed 616 persons, their toll being particularly heavy—441 deaths—among men age 45-64. They struck indiscriminately among managerial and supervisory personnel, technical and clerical employees, skilled, semi-skilled and unskilled.

These findings are quite typical for the United States today. They have been repeatedly recorded in longterm prospective epidemiologic studies, such as the one being conducted by our group in the labor force of the People's Gas, Light and Coke Company and that of colleagues in the Western Electric Company in Chicago, in Framingham, New York City, Tecumseh, Albany, Wilmington, Charleston, San Francisco, Los Angeles, etc.

A more detailed review of the cardinal findings of these investigations serves to highlight the key challenges confronting medicine and public health today. The research in the People's Gas Company began in 1957. Extensive data on the male labor force age 40-59 were collected and analyzed in 1958. The findings, it is appropriate to reiterate, well represent the situation in this country today. Almost one-third of the middle-aged men were found to have one or more detectable abnormalities of the cardiovascular system (Fig. I). In many cases it was "only" elevated blood pressure, without any demonstrable abnormalities in the blood vessels. In 182 per thousand men (almost 20%), there was demonstrable disease in blood vessels. In 46 per thousand, hypertensive heart disease was present; in another 46 per thousand, atherosclerotic coronary heart disease. These two separate but interrelated processes—hypertension and atherosclerosis—are the major cardiovascular problems today. Note also the sizeable group of individuals who, because of their symptoms or their electrocardiographic findings, were evaluated as having suspect coronary disease (Fig. I). A definitive diagnosis could not be made, but there was enough evidence of disease so that they could not be given a clean bill of health.

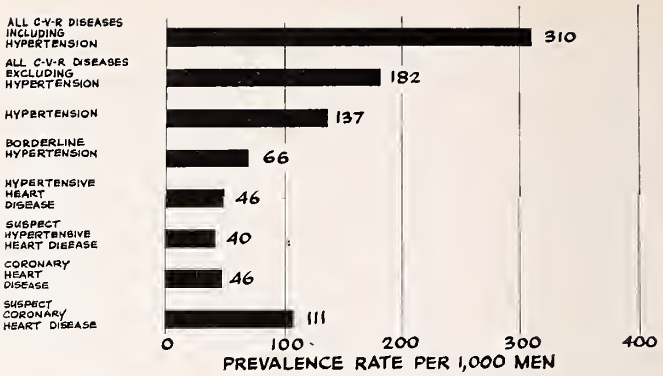


Figure I

Prevalence of Cardiovascular-Renal Diseases in the 1465 men age 40-59 in the Peoples Gas Light and Coke Company labor force, 1958.

The data in Figure I present a "still picture" of the disease situation in a population at a given point in time. For both practical and research reasons, it is at least as important to get a "moving picture," that is, an analysis of the rate of development of new disease over time in persons orginally healthy. Of the 1465 middle-aged men in the Chicago Utility Company Study, 1329—with no history of heart attack at the time of initial examination in 1958—have been followed in detail without systematic intervention by the research group during the subsequent years. Data analyzed to date indicate that the 40 month incidence rate of new coronary disease was in the order 35 per 1000 men, of about 11/1000/year. With simple arithmetic, it is possible to arrive at the approximation that the average presently healthy middle-aged American male, free of clinical coronary disease (insofar as

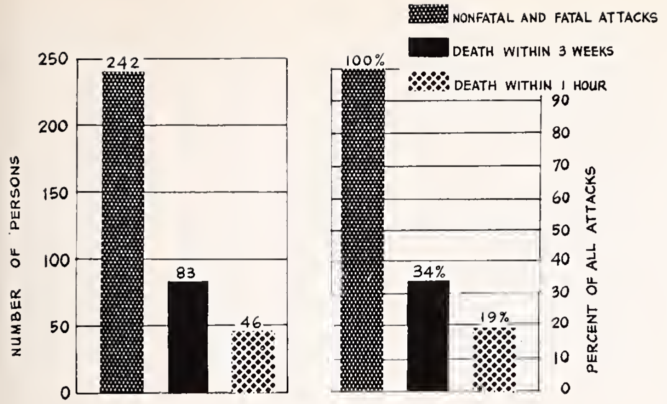


Figure II

Immediate mortality in heart attacks among 5128 men and women age 30-62 at the onset of the Framingham prospective epidemiologic study—eight year follow-up data.

can be determined with our present diagnostic methods), has about one chance in five of developing this disease in middle-age, that is, before age 65. This is indeed a rather high average risk.

An incidence rate of about 10-15 per thousand per year is fairly uniformly experienced by all subgroups in our middle-aged urban male population—by Negro and white men; indoor and outdoor workers; men doing sedentary or light or medium activity work; white collar and blue collar workers (with a statistical hint that the blue collar semiskilled, unskilled and service workers may be a little better off, but not remarkably so). Contrary to earlier misconceptions, the recent studies in representative large samples of the living population have yielded solid consistent data showing that the toll being exacted by coronary disease is falling heavily upon all socioeconomic and ethnic strata. This disease is by no mean confined to the managerial, executive, supervisory groups. It is indeed "epidemic," to use Dr. Paul Dudley White's term, throughout our middle-aged male population.

Figure II illustrates a further important characteristic of this disease. These are data recently presented at the Fourth World Cardiological Congress in Mexico City. They are based on several years of follow-up by the Public Health Service Study of more than 5,000 men and women in Framingham, Massachusetts. They document a particularly pernicious aspect of the coronary disease problem. Our studies of the Gas Company men have yielded like findings. In the 5,000 Framingham men and women, originally free of coronary disease, 242 developed the disease over time. Of the 242, 83 (34%) died within three weeks of becoming ill; 46 (19%) experienced sudden death, occurring within one hour, that is within such a short time as virtually to preclude their receiving any medical care whatsoever. These facts deserve emphasis, because they compel an important conclusion: If effective progress is to be made against this disease, if a real breakthrough is to be achieved, a significant lowering of its impact, at least in middle age (as a first objective), then of necessity—in view of the high rate of sudden death—the focus of the effort must be on primary prevention. That is the prevention of the first attack! As important as it is to improve therapy during the acute attack (for those surviving long enough to receive medical care), as important as it is to improve long-term therapy for those who fully recover from an acute attack—and the importance of these cannot be overestimated—the major emphasis must be on primary prevention.

The validity of this conclusion is driven home by an additional set of related facts: Those who recover from an acute episode of coronary disease in middle age have a subsequent mortality risk several times greater than the general population of age-sex-matched individuals. Data demonstrating this phenomenon have been repeatedly collected in life insurance company studies, as well as in prospective epidemiological and long-term clinical investigations. Data from the Gas Company study and the placebo group in our long-term evaluation of estrogen therapy fully confirm these findings (Figs. III and IV).

All these facts—about the high mortality rate with acute first attacks of myocardial infarction and the impaired long-term prognosis of those fortunate enough to recover from the immediate onslaught of the disease—serve to focus the spotlight on the foremost present-day challenge: Is it possible—is the knowledge available—to accomplish primary prevention of premature clinical coronary disease? That is, can first attacks be prevented at age 40, 50 or 60?

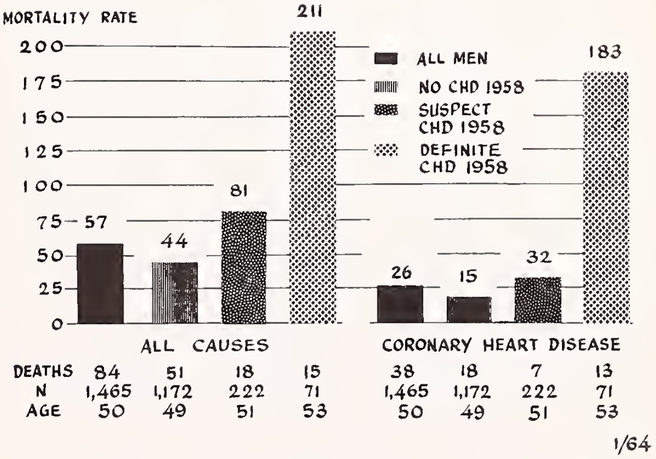


Figure III

Relationship between diagnostic status with respect to Coronary Heart Disease in 1958 and subsequent mortality—Peoples Gas Light and Coke Company Study, men originally age 40-59, January 1, 1958 through October 31, 1963.

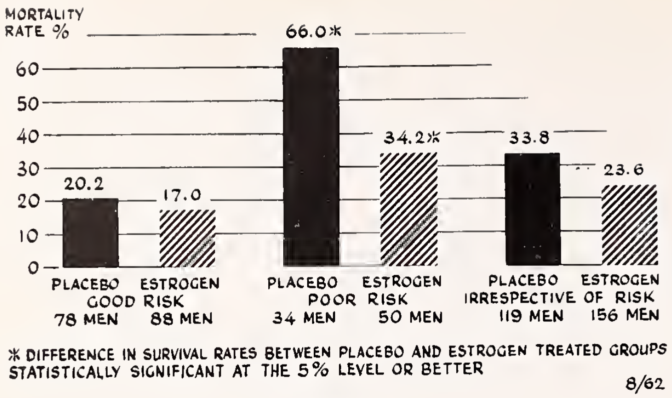


Figure IV

Five year mortality rate in men with a history of previous Myocardial Infarction prior to the age of 50. Good risk men are those with a single previous myocardial infarction uncomplicated by other major diseases or by friction rub, arrythmia, shock, congestive heart failure or extension of the infarct during the acute episode; poor risk men are those with two or more previous myocardial infarctions, or men with other major diseases, or men with a single previous myocardial infarction complicated by friction rub, arrythmia, shock, congestive failure or extension of the infarct during the acute episode.

The Possibility of Achieving Primary Prevention Of Premature Clinical Coronary Heart Disease

With regard to this key question, one of the remarkable achievements of recent research is the identification of factors influencing risk of developing this disease, and, based on this, the development of the ability to find susceptible individuals before they become sick, and to intervene in an effort to decrease their coronary proneness.

It is an axiom of preventive medicine that in order to develop truly effective programs of primary prevention, it is essential to focus and concentrate the effort against the susceptibles. In polio, for example, children and pregnant women are susceptible. Therefore—while an effort is made to immunize the entire population—particular attention is devoted to inoculating the susceptibles.

Therefore, one of the major advances in the field of coronary disease in recent years is the recognition that people vary markedly in their susceptibility to this disease. The data on ability to detect susceptibles demonstrate that the figure on the average risk of the average American male—one chance in five of developing a heart attack in middle age—is, like many averages, an abstraction of only limited meaning. It is an average of very different risks, for there are in the American population those who have findings indicating marked susceptibility, as high as one chance in two or two chances in three or worse of developing coronary disease before age 65. At the other end of the distribution, there are more fortunate individuals with a risk of only one in 20, one in 30 or one in 40.

A corollary and byproduct of this achievement in assessing susceptibility is the ability to identify coronary prone individuals before they develop overt clinical disease. The methods for making this assessment of risk are quite simple. They entail making a set of standard medical measurements.

The first point worth re-emphasizing with respect to coronary-proneness is the remarkably greater susceptibility of men compared to women, particularly prior to age 45, that is prior to the onset of menopause in women. Middle-aged women, particularly white women, are in general highly resistant to this disease. (Table VIII). This female resistance to heart attacks is the single main factor accounting for the six year greater life expectancy of women than men in the United States today. The fact that in the population of the United States there are more women than men, the fact that early widowhood is a major social problem, is attributable first and foremost to the impact of coronary disease on men. In the Framingham study, there were no heart attacks in women under age 40, whereas there were 21 per thousand in men (Fig. V). The contrast was similar for the age group 40 to 49. This sex differential began to lessen only in the age group 50 to 59, and gradually decreased thereafter. First of all, therefore, in the evaluation of risk, it is essential to recognize that men are generally more susceptible than women. This fact, however, should not be exaggerated, since women after the menopause develop an increasing coronary proneness, as is evident from the above-cited statistics (Table VIII and Fig. V). It is not possible in this report to digress and describe the research done on the role of internal secretions—particularly the estrogenic hormones of the ovary—in protecting women prior to the menopause. (See references 10-12).

The relationships between two key variables—blood pressure and serum cholesterol level—and

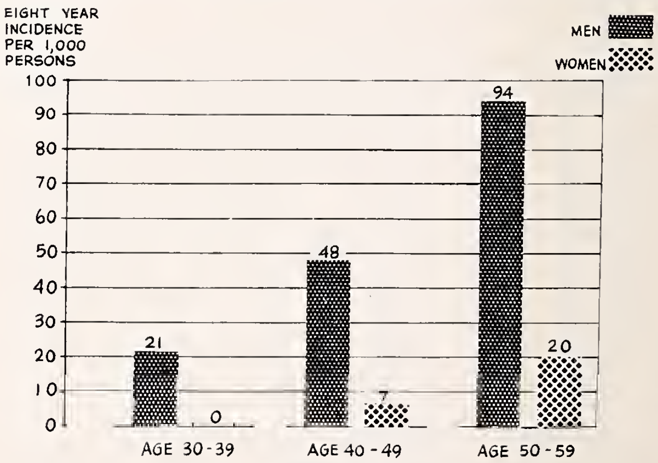


Figure V

Eight-year incidence of heart attacks in Framingham Study, men and women age 30-59 at entry.

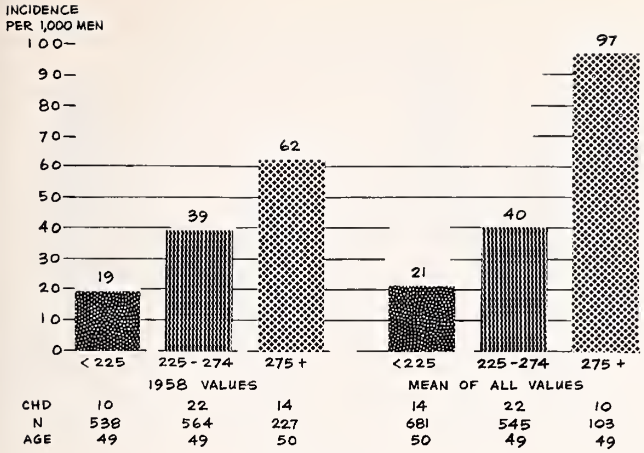


FIGURE VI

Relationship between serum cholesterol level and incidence of Coronary Heart Disease in the Peoples Gas Light and Coke Company Study, 1958-1962. The 1958 values represent a single determination on each man. The mean of all values represents a mean of all available data for each man, assessed at intervals from 1958 to 1962.

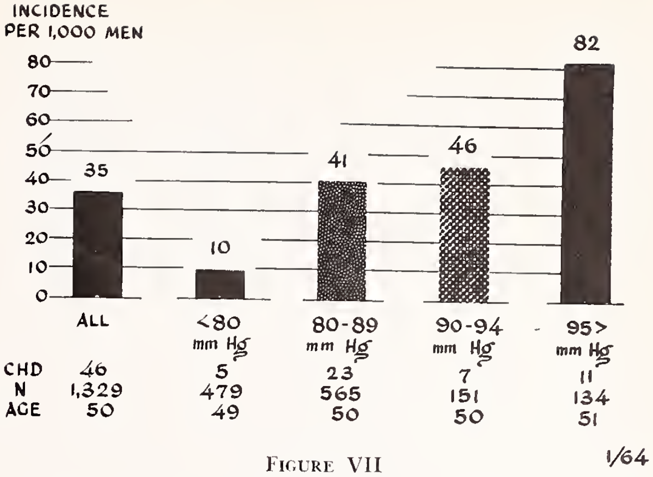


FIGURE VII

Relationship between diastolic blood pressure in 1958 and incidence of Coronary Heart Disease, 1958-62, in the Peoples Gas Light and Coke Compnay men age 40-59 in 1958.

coronary proneness are illustrated in Table IX and Figures VI-VIII. Men with elevated blood pressure had a manifold greater risk of developing coronary disease than men with normal blood pressure. Men with high serum cholesterol levels developed three to five times as many heart attacks as men with lower serum cholesterol levels. Those normal with respect to both factors had only 10 heart attacks per thousand in 40 months—a risk of about one in 20 of developing coronary disease before age 65. Those with both these abnormalities had seven- to nine-fold higher incidence rates, amounting to a risk of about one chance in three or worse of de-

TABLE VII

DEATH RATES, ALL CAUSES, CARDIOVASCULAR-RENAL AND NON-CARDIOVASCULAR-RENAL DISEASES, U. S. POPULATION, AGE 55-64 BY SEX AND COLOR, 1920-1959

		DEATH RATE PER 100,000 POPULATION				
CAUSES	YEAR	BOTH SEXES, ALL RACES	WHITE MALE	WHITE FEMALE	NON-WHITE MALE	NON-WHITE FEMALE
All Causes	1920	2359	2421	2171	3114	3580
	1930	2403	2552	1993	4039	4143
	1940	2216	2522	1684	3711	3318
	1950	1901	2304	1294	3481	2763
	1959	1712	2203	1064	3211	2405
Cardiovascular-Renal Diseases	1920	1040	1056	956	1449	1730
	1930	1140	1200	913	2170	2311
	1940	1122	1305	793	1992	1955
	1950	1068	1337	664	1995	1760
	1959	939	1262	518	1795	1467
Non-Cardiovascular-Renal Diseases	1920	1319	1365	1215	1665	1850
	1930	1263	1352	1080	1869	1832
	1940	1094	1217	891	1719	1363
	1950	833	967	630	1486	1003
	1959	773	941	546	1416	938
Per Cent Change, All Causes	1920-1959	−27.4%	− 9.0%	−51.0%	+ 3.1%	−32.8%
	1940-1950	−14.2%	− 8.6%	−23.2%	− 6.2%	−16.7%
	1950-1959	− 9.9%	− 4.4%	−17.8%	− 7.8%	−13.0%
Per Cent Change, CVR Diseases	1920-1959	− 9.7%	+19.5%	−45.8%	+23.9%	−15.2%
	1940-1950	− 4.8%	+ 2.5%	−16.3%	+ 0.2%	−10.0%
	1950-1959	−12.1%	− 5.6%	−22.0%	−10.0%	−16.6%
Per Cent Change, Non-CVR Diseases	1920-1959	−41.4%	−19.7%	−55.1%	−15.0%	−49.3%
	1940-1950	−23.9%	−20.5%	−29.3%	−13.6%	−26.4%
	1950-1959	− 7.2%	+13.3%	−13.3%	− 4.7%	− 6.5%

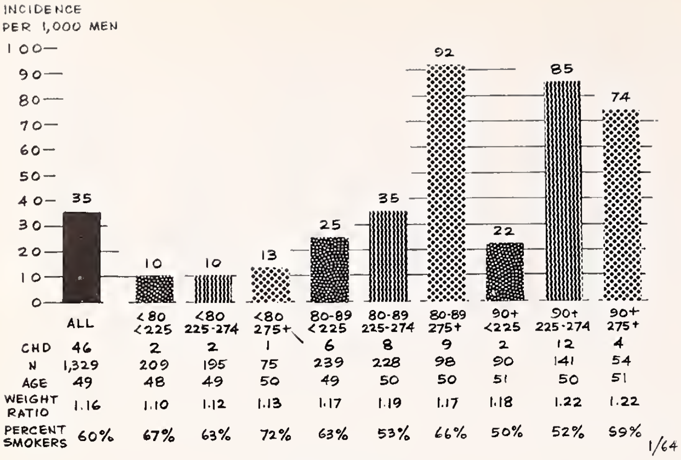
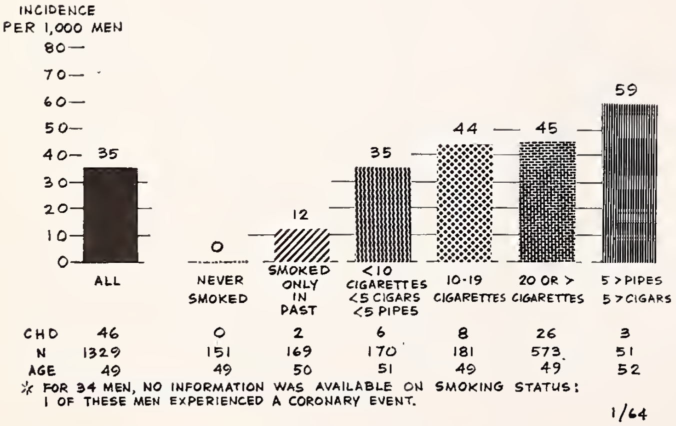


FIGURE VIII

Relationship between diastolic blood pressure, serum cholesterol and incidence of Coronary Heart Disease, 1958-1962, Peoples Gas Light and Coke Company men age 40-59 in 1958.

veloping a heart attack in middle age. These are some of the high risk men in the U. S. population.

Another important factor influencing risk is smoking, particularly cigarette smoking (Fig. IX). Note that no coronary events occurred during the first 40 months of follow-up, from 1958 to 1962, in the 151 men who never smoked. Among the 169 men who had quit by 1958, while they were still free of disease, only two coronary episodes ensued, giving a low rate of 12/1000 men in 40 months, or less than 4/1000/year, i.e. about one-third the average rate. Smokers faired far worse, exhibiting rates three to five times higher than those who had quit smoking.



* FOR 34 MEN, NO INFORMATION WAS AVAILABLE ON SMOKING STATUS; 1 OF THESE MEN EXPERIENCED A CORONARY EVENT.

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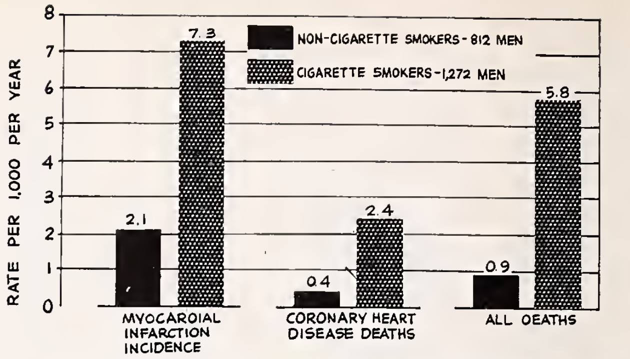
FIGURE IX

Relationship between smoking and incidence of Coronary Heart Disease, 1958-1962, Peoples Gas Light and Coke Company men age 40-59 in 1958.



ALBANY FOLLOW-UP PERIOD -- 6 YEARS, FRAMINGHAM -- 8 YEARS. RATES C
MYOCARDIAL INFARCTION INCIDENCE AND CORONARY HEART DISEASE DEATI
ARE ADJUSTED TO ASSESS CONTRIBUTION OF CIGARETTE SMOKING INDEPEN
OF CHOLESTEROL, WEIGHT AND BLOOD PRESSURE.

FIGURE X

Relationship between smoking and incidence of Myocardial Infarction, Coronary Heart Disease mortality and mortality from All Causes, men age 40-49, Framingham and Albany Studies. Albany follow-up period—6 years, Framingham—8 years. Rates of Myocardial Infarction incidence and Coronary Heart Disease death are adjusted to assess contribution of cigarette smoking independent of cholesterol, weight and blood pressure.

Many other studies in Great Britain and the United States have reported similar findings; data from one of these are presented in Figure X. Note the six-fold difference in total death rates between non-cigarette smokers and cigarette smokers. Note also that these data from the Framingham and Albany studies, involving several thousand men followed for six and eight years respectively (the death rates are given as deaths per thousand men per year), demonstrate a more than six-fold difference in fatality rate from myocardial infarction, or heart attack in cigarette smokers vs. non-cigarette smokers, and a difference in rate of all heart attacks (fatal and non-fatal) that is more than three-fold. These statistics deserve to be carefully pondered.

Few people appreciate that cigarette smoking is a twentieth century habit. As a mass phenomenon, it in no sense dates back to Sir Walter Raleigh. Its

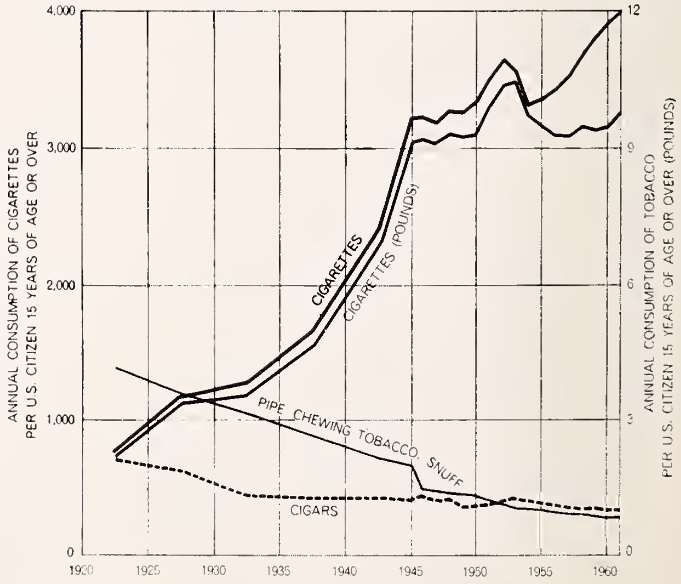


FIGURE XI

Changes in tobacco use, 1920-60.

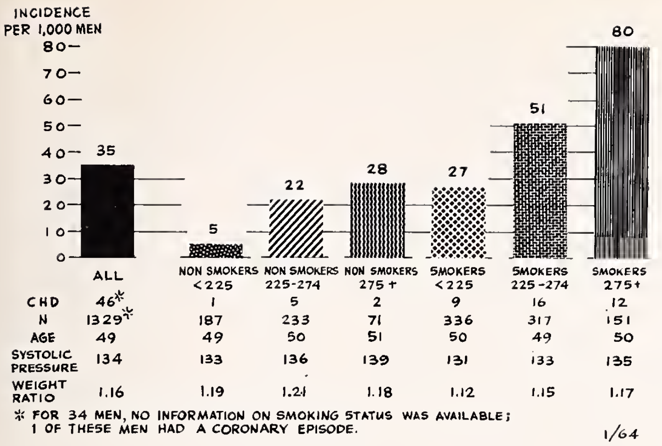


Figure XII

Relationship between smoking, serum cholesterol level in 1958 and incidence of Coronary Heart Disease, 1958-1962, Peoples Gas Light and Coke Company men age 40-59 in 1958.

first prerequisite was the invention of machines for large scale manufacture of cigarettes, a development that occurred toward the end of the nineteenth century. The second prerequisite was the adoption of the habit en mass, an event occurring during and after World War I (Fig. XI).

Considerable research evidence is available indicating that this development is one among three parallel alterations in the American way of life—changes in habit patterns which together have contributed significantly to the increased incidence of premature atherosclerotic coronary heart disease in the U. S. population. The other two are the inexorably developing habits of physical inactivity and excessive ingestion of diets high in saturated fats and cholesterol.

The prospective epidemiologic data further reveal that when smoking is combined with hypercholesterolemia, or with overweight, the risks rise proportionately, and the difference in coronary proneness between persons not stigmatized by these abnormalities and those demonstrating these risk factors are several fold (Figs. XII and XIII). When the analysis is extended to include simultaneously status with respect to four risk factors—hypercholesterolemia, hypertension, smoking and overweight—then the range of risks is very great indeed (Table X).

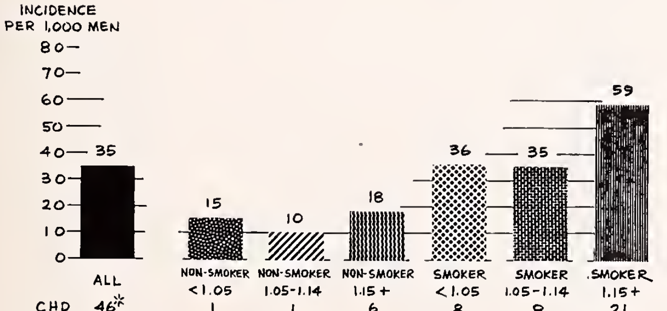


Figure XIII

Relationship between weight, smoking and incidence of Coronary Heart Disease, 1958-1962, Peoples Gas Light and Coke Company men age 40-59 in 1958.

Up to this point, consideration has been given to findings that are not direct measurements of the status of the heart or coronary arteries *per se*. Rather, they are measurements of physiological variables (blood pressure, weight, serum cholesterol) known to influence the development of atherosclerosis. These variables are therefore properly designated as coronary risk factors. Other coronary risk factors include diabetes, thyroid disease, kidney abnormalities, lack of exercise, and a history of blood vessel disease (atherosclerosis, hypertension) occurring prematurely (before age 60) in members of the family.

Medicine has also increased its knowledge in another area of vital importance for predicting risk of developing frank clinical coronary disease. It has been definitely shown that certain abnormalities revealed by the electrocardiogram — abnormalities frequently found during routine examination of presumably healthy people—also portend an increased likelihood of developing heart attacks during the ensuing years. The electrocardiogram is therefore an invaluable means of assessment, of detecting persons with coronary disease before they have developed symptoms and become clinically ill. The electrocardiogram gives direct information concerning the status of the heart. Several abnormalities demonstrable by the electrocardiogram are

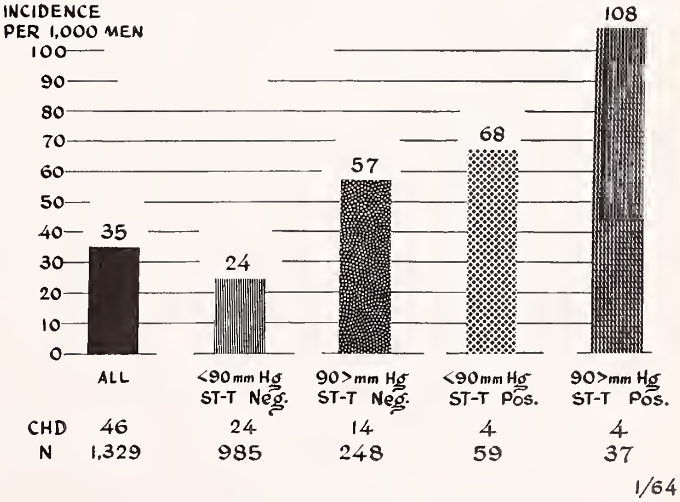


Figure XIV

Relationship between diastolic blood pressure, non-specific ST-T abnormalities and incidence of Coronary Heart Disease, 1958-1962, Peoples Gas Light and Coke Company men age 40-59 in 1958.

Table VIII
Mortality Rates Per 100,000 Population, 1950 and 1960
All Causes and Major Cardiovascular Renal Causes by Age-Sex-Color

Age-Sex-Color Group	All Causes		Cardiovascular-Renal Diseases		Arteriosclerotic Heart Disease		Arteriosclerotic and Degenerative Heart Disease		Hypertensive Disease		Cerebro-vascular Diseases	
White Males	1950	1960	1950	1960	1950	1960	1950	1960	1950	1960	1950	1960
45-49	660.4	709.3	374.6	347.9	236.4	254.9	255.3	262.1	27.2	13.4	37.9	28.7
50-54	1,089.0	1,183.3	653.0	625.6	417.2	462.6	449.6	478.9	55.0	25.7	70.9	54.7
55-59	1,734.7	1,784.6	1,065.5	989.8	667.3	719.0	730.2	746.2	93.9	46.4	131.8	97.1
60-64	2,642.4	2,751.4	1,659.1	1,590.5	985.3	1,119.1	1,101.7	1,172.6	149.0	78.4	242.0	189.1
White Females												
45-49	411.5	368.5	161.3	109.0	43.5	40.8	53.5	43.9	24.9	9.9	41.1	25.3
50-54	622.5	560.3	277.9	198.0	91.7	85.6	108.8	92.0	47.8	18.7	70.1	43.3
55-59	978.0	829.7	488.6	357.0	185.7	183.6	219.7	195.6	75.6	34.4	116.4	69.0
60-64	1,568.6	1,362.2	878.9	706.2	364.3	384.4	432.5	411.9	137.2	67.8	204.8	141.6
Non-White Males												
45-49	1,264.9	1,241.5	640.1	546.1	182.7	224.8	238.2	244.1	150.2	106.1	141.2	119.9
50-54	2,139.7	1,916.2	1,217.1	923.3	339.8	382.1	463.1	419.3	287.5	170.2	279.7	200.1
55-59	2,936.0	2,500.5	1,729.4	1,338.3	491.4	556.1	659.1	626.1	384.3	233.0	419.4	313.3
60-64	3,738.8	4,053.8	2,384.5	2,293.0	634.4	956.0	911.8	1,090.5	503.1	376.1	556.0	547.2
Non-White Females												
45-49	1,208.1	919.4	666.1	436.1	124.2	124.7	176.3	138.0	189.0	106.3	189.7	121.2
50-54	1,890.0	1,419.5	1,107.8	738.3	217.4	220.7	304.8	253.2	308.0	176.4	312.4	207.9
55-59	2,350.2	1,951.8	1,478.2	1,138.7	302.5	366.2	446.3	361.0	402.8	249.9	416.5	330.4
60-64	3,180.3	3,019.5	2,126.3	1,889.0	450.3	636.9	676.3	559.1	549.4	392.0	618.3	561.0

indicative of damage to the heart probably due to atherosclerosis of the coronary arteries supplying blood to the heart muscle (Fig. XIV). When these abnormalities are encountered in apparently healthy people (as is often the case), they are therefore warning signals that frank heart attack is more likely to occur.

In the Framingham study, an assessment was made of the relationship of three measurements—the electrocardiogram, blood pressure and serum cholesterol—and risk of developing frank clinical coronary disease. Those men normal with respect to all three of these experienced very few heart attacks in the ensuing years. Those with one abnormality experienced a twelve-times higher attack rate; those with two abnormalities, a twenty-times higher rate; those with all three abnormalities, a thirty-three-times higher rate! These statistics illustrate with a vengeance the value of these measurements in detecting coronary prone persons—and the challenge to preventive medicine such persons present!

The next relevant question is: How frequently are coronary prone persons encountered in the population? The studies of middle-aged men employed by the Peoples Gas Light and Coke Company have yielded highly significant data on this matter—again, data typifying the general situation prevailing throughout this country today. Over 500 men per thousand were found to be overweight, 284 per thousand markedly overweight; 283 per thousand had a high serum cholesterol level; 103 per thousand had frank high blood pressure; more than 400 per thousand were heavy smokers; 175 per thousand had a positive family history of premature blood vessel disease (Fig. XV).

Men with two or three risk factors were frequently encountered (Table X). This is—let it be emphasized—a typical contemporary American situ-

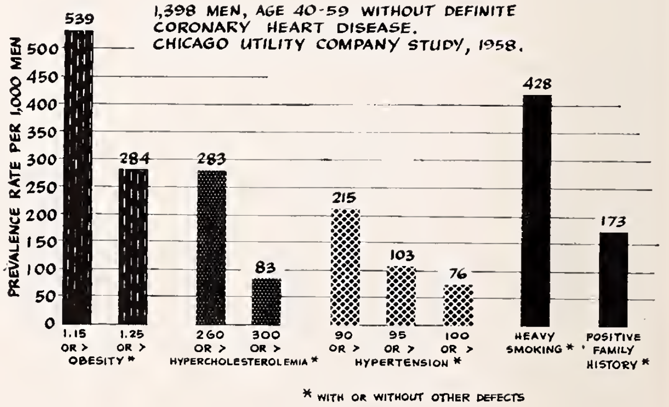


Figure XV

Prevalence of abnormalities associated with increased susceptibility to Coronary Heart Disease, 1398 men age 40-59 in 1958 without definite Coronary Heart Disease—Peoples Gas Light and Coke Company Study.

ation. Let not the Gas Company be stigmatized—its labor force is "par for the course." At the other end of the risk spectrum, men free of multiple abnormalities are all too rare. Among the middle-aged employees at the Gas Company, only 136 of 1,465 men (9.3%) had normal serum cholesterol, weight and blood pressure (all three combined); further exclusion of diabetics, heavy smokers and men with a positive family history left only 48 men (3.3%) normal with respect to all six risk factors!

The next logical step in the argument is a relatively simple one: Something can be done about most of these abnormalities. True, for the sake of preventing heart attacks it is not reasonable to feminize men with estrogenic hormones. Nor is it possible, so far, to influence genetic background and at that level counteract the influence of family history. However, even with respect to family history, there is no reason for fatalistic hopelessness. For it is now known that to a large degree the familial tendency to premature coronary disease results from familial tendencies to high serum cholesterol, to obesity, to high blood pressure, to diabetes—familial tendencies that seem to be in many cases partly genetic and partly environmental in origin. And it is quite possible for contemporary medicine to treat every one of these abnormalities, if they are recognized early, that is, before frank coronary disease has occurred. It is therefore possible to intervene and attempt to head off the effect of a poor family background.

In any case, the coronary risk factors are often present without a positive family history, and are highly amenable to effective medical therapy. High blood pressure can today be successfully treated by diet and safe new drugs, particularly when it is detected early, before the hypertension is severe, and serious organ damage has developed. Obesity can also be treated by reliable, professional methods, although its long-term control is a tough problem. Heavy smoking, particularly cigarette smoking, can be eliminated, although it too is a tough problem. It is now known that elevated serum cholesterol can be lowered in most cases by dietary means entirely compatible with continued enjoyment of the pleasure of good eating. Diabetes is also capable of being controlled, as are other coronary risk factors.

It is a simple logical conclusion that if these abnormalities make for increased likelihood of heart attacks, and these abnormalities can be detected before attacks occur, and corrected and controlled, then the possibility arises of preventing heart attacks. How valid is this logical possibility? Here it is necessary at present to give an interim answer. Several sets of data are available which are very encouraging in this regard. For example, data are available indicating that heavy cigarette smokers who quit before they became ill will in due course experience a decline in coronary proneness down toward the risk of non-cigarette smokers (Figs. IX, XVI). This is indeed a very encouraging fact.

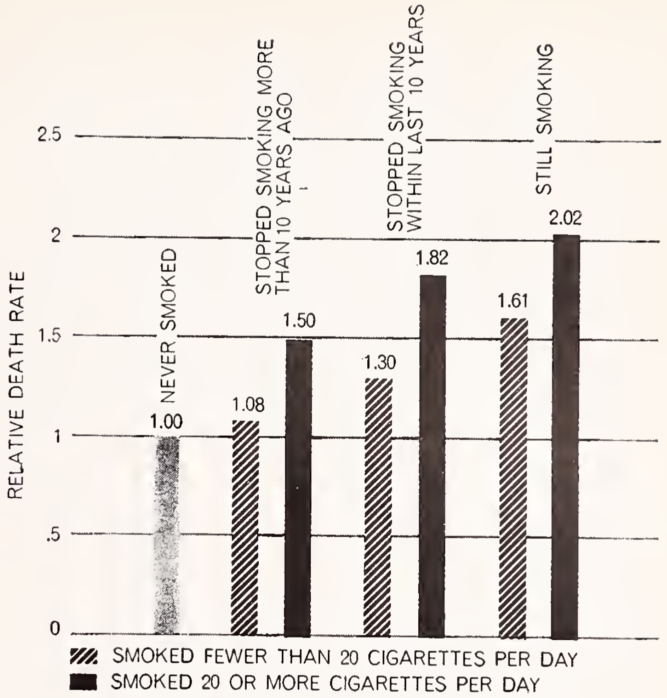


FIGURE XVI

Relative death rates in former smokers, compared with persons who never smoked and those still smoking.

Life insurance data are also available indicating that obese men who reduce and stay reduced (in order to be re-rated at standard rates by their insurance companies) also have a subsequent mortality experience like that of non-overweight men. Data collected during the last five or ten years of the use of the new drugs for the treatment of hypertension indicate that modern effective control of high blood pressure leads to reduced incidence of heart attacks, heart failure, strokes and kidney failure—the complications that produce illness and premature death in hypertensives. As a result of the control of high blood pressure by diet and the new drugs, hypertensives are now living longer.

While it is a debatable question, there is evidence indicating that well controlled diabetics suffer significantly less from the major complications of diabetes (heart attacks, strokes and other vascular complications) than do poorly controlled diabetics. Finally there is considerable evidence collected in central Europe after World War I and in the occupied countries during World War II, indicating that the changes in diet, exercise and smoking under wartime conditions were associated with significant declines in mortality rates from heart attack. All these intriguing pieces of information support the logical conclusion that treatment of coronary risk factors may be effective in preventing the disease.

When the American Heart Association a few years ago arrived at the conclusion that the available data warranted a statement on diet, heart attacks and strokes, they issued such a statement to the profession and the public. This statement was very carefully formulated so as to be neither too negative nor too positive, based on the data available. This statement emphasized the possibility of prevention—not the certainty at this juncture, because the data available today are not yet comprehensive enough to warrant our speaking about the certainty of prevention—"merely" the possibility. The more recent statement of the A.H.A. on smoking and its negative cardiovascular effects was in a similar vein.

Research And Developmental Efforts On The Prevention Of Premature Clinical Coronary Disease

In order to clarify this current situation, an analogy is useful, since it has considerable validity. The problem of preventive approaches to coronary disease stands today at the point where polio research stood in 1953. By that time, the polio researchers had isolated the viruses, learned how to grow them, learned how to kill them without destroying their ability to provoke antibodies, had shown that this vaccine could be safely given, that it did provoke antibodies in man and that it did protect monkeys against paralytic polio. "All" that had to be done was a mass field trial to test whether such a vaccine did protect children in the mass against the disease. The National Foundation, the Public Health Service, Dr. Jonas Salk, Dr. Thomas Francis, and their research teams did such a mass field trial and the results are history. Similar mass field trials are now needed to test the ability to achieve effective primary prevention of heart attacks by nutritional, hygienic and pharmacologic means.

The mass field trials needed in the coronary disease field are essentially similar in their basic principles to those needed for polio. However, specific features of the disease put a special stamp on the field trials against coronary disease. The preventive measures are not vaccines, rather changes in living habits; the subjects are not children, rather middle-aged men; the period of follow-up is not one summer, rather four to five years. These concrete aspects create unique problems for mass field trials on coronary disease and render them quite difficult.

Since 1957 pilot studies along this line have been in progress, and by now, considerable experience has been accumulated, in Chicago, New York, Cleveland, Los Angeles, and elsewhere. Our Coronary Prevention Evaluation Program in Chicago works longterm with high-risk men age 40-59. It strives to correct, and keep corrected—the decisive challenge — five abnormalities making for coronary-proneness, namely overweight, high serum cholesterol, high blood pressure, heavy cigarette smoking and lack of exercise. The research physicians and nutritionists work closely with the men and their wives to effect a permanent change in living habits, particularly eating, exercise and smoking habits. Short-lived efforts—the frequent American pattern of going on a diet, and then going off—are futile. A sustained correction—for years—of high blood cholesterol, overweight, etc., must be achieved, if anything is to be accomplished in the way of preventing heart attacks.

The dietary approaches required to attain these goals have been worked out in great detail. In the language of nutrition, they involve diets moderate in total calories, total fats, polyunsaturated fatty acids and carbohydrates; low in saturated fatty acids and cholesterol; and high in all essential nutrients (proteins, amino acids, vitamins, minerals) (Table XI). In terms of foodstuffs this means (Table XII):

Emphasizing the low-fat dairy products (skim milk, buttermilk, cottage cheese), and de-emphasizing the high-fat (sweet cream, sour

Table IX
Diastolic Blood Pressure (1958) and Disease Incidence
1329 Men Age 40-59 on Jan. 1, 1958 — Chicago Utility Co. Study

	No. and Rate of Events									
Events	< 80 mm Hg. 479 Men		80-89 mm Hg. 565 Men		90-94 mm Hg. 151 Men		95 > mm Hg. 134 Men		All 1329 Men	
All Deaths 1/1/58-10/31/63	16	33.4	22	38.9	8	53.0	17	126.9	63	47.4
CHD Deaths 1/1/58-10/31/63	3	6.3	10	17.7	3	19.9	6	44.8	22	16.6
Stroke Deaths 1/1/58-10/31/63	2	4.2	4	7.1	1	6.6	3	22.4	10	7.5
CHD Deaths 1958-62	2	4.2	5	8.8	0	....	3	22.4	10	7.5
CHD Incidence 1958-62	5	10.4	23	40.7	7	46.4	11	82.1	46	34.6
MI Incidence 1958-62	2	4.2	12	21.2	6	39.7	4	29.9	24	18.1

TABLE X

RELATIONSHIP BETWEEN FOUR CORONARY RISK FACTORS (SERUM CHOLESTEROL, BLOOD PRESSURE, WEIGHT, SMOKING) AND CORONARY HEART DISEASE

CHICAGO UTILITY CO. STUDY, 1958-62

RISK FACTOR STATUS	NO. OF MEN	CORONARY DISEASE INCIDENCE	
None Positive	94	1*	10.6†
Smoking Only	260	8	30.8
Overweight Only	161	0	....
Any One Only of Three (Overweight, Hypertension, Hypercholesterolemia)	227	2	8.8
Any One Factor Only of All Four	487	10	20.5
Smoking + Obesity – 2 Only	169	4	23.7
Smoking + Hypercholesterolemia – 2 Only	125	4	32.0
Any 2 Only of 3 (Overweight, Hypertension, Hypercholesterolemia)	159	4	25.2
Any 2 Only of All 4	484	12	24.8
Smoking + Overweight + Hypercholesterolemia	90	5	55.6
Smoking + Overweight + Hypertension	55	6	109.1
Overweight + Hypertension + Hypercholesterolemia	45	2	44.4
Any Three Only	222	17	76.6
All Four Positive	42	6	142.9
Any Three or All Four	264	23	87.1
All	1329	46	34.6

* No. of Men † Incidence rate per 1000 men.

Cutting points: Overweight—observed weight/desirable weight 1.15 >; hypercholesterolemia — 1958 value 250 mg. per 100 ml. >; hypertension — lowest diastolic in 1958 90 >; Smoking — 10 or > cigarettes per day.

cream, ice cream, whipped cream, cheeses, butter).

Emphasizing lean non-marbled cuts of meat and poultry, and de-emphasizing the fat marbled cuts, with trimming off fat before cooking, cooking so as to get rid of fat (broiling, rotisserieing, roasting with discarding of drippings, letting stews and soups stand in the refrigerator overnight and skimming off congealed fat); use of vegetable oils in braising or basting meats, etc.; moderation of meat portion size (four to six ounces, not twelve to sixteen).

Emphasizing fish and sea food; de-emphasizing eggs.

Emphasizing vegetable oils, and de-emphasizing solid table spreads (butter, margarines) and solid shortenings (lard, suet, hydrogenated vegetable fats, drippings).

Emphasizing fruit desserts (citrus and non-citrus), and de-emphasizing commercial cakes, pastries, shortcakes, cookies and pies.

Emphasizing green and yellow vegetables and legumes (peas, beans).

Emphasizing moderation in use of starches (potatoes, rice, spaghetti, breads, cereals), carbohydrate-rich spreads (jellies, jams, honey, marmalade), sweets and alcoholic beverages.

Pages and pages of delightful and tempting recipes are available—to convince even the most skeptical that pleasure lies ahead along this way of good hope for the prevention of heart attacks. Indeed, one of the major lessons of the research experience to date is its demonstration that one of the pleasures of the good life—the pleasure of good eating—can and should remain as the effort proceeds to end the contemporary epidemic of premature heart attacks.

From the experience of the Coronary Prevention Evaluation Program to date, and similar studies, it is reasonable to conclude that a majority of high-risk middle-aged American males can be won for effective cooperation in an effort to prevent heart attacks. Moreover, there is no doubt that the cardinal risk factors can be corrected and kept corrected (Table XIII). Significant progress has also been registered in breaking the cigarette smoking habit, and in developing patterns of regular exercise.

TABLE XI

OVERALL CHANGES IN DAILY NUTRIENT INTAKE — TOTAL EXPERIENCE OF 99 PARTICIPANTS IN CORONARY PREVENTION EVALUATION PROGRAM

NUTRIENT	CONTROL	TREATMENT
Total calories	2465 ±692.4*	1668 ±334.4
Carbohydrate (gm.)	230 ± 73.3	192 ± 49.3
Protein (gm.)	106 ± 31.8	95 ± 17.1
Total fat (gm.)	119 ± 42.7	56 ± 14.9
Saturated fatty acids (gm.)	48 ± 19.0	19 ± 5.7
Unsaturated fatty acids (gm.)	66 ± 23.5	34 ± 9.7
Polyunsaturated fatty acids (gm.)	16 ± 6.9	12 ± 4.6
Cholesterol (mg.)	627 ±219.7	307 ± 93.8
Percentage of calories from carbohydrate	37.7± 7.1	46.3± 6.3
Percentage of calories from protein	17.7± 3.7	23.4± 3.5
Percentage of calories from total fat	43.0± 6.2	29.7± 5.3
Percentage of calories from sat. fatty acids	17.3± 3.3	10.1± 2.3
Percentage of calories from unsat. fatty acids	24.0± 3.5	18.3± 3.4
Percentage of calories from polyunsat. fatty acids	5.8± 1.9	6.7± 2.0
Ratio: Polyunsat. fatty acids / sat. fatty acids	0.36± 0.15	0.80± 0.33

* Standard deviation of the mean.

Based on these positive experiences, and similar ones in New York, Los Angeles, Cleveland and elsewhere, a national cooperative study has been organized to explore further the feasibility of mass field trials to prevent heart attacks. The first studies along this line have been proceeding well for several months now. Grants have been awarded for this purpose by the National Heart Institute, close cooperation and support have been forthcoming from the American Heart Association and its affiliates, and work is proceeding in Chicago, Baltimore, Boston, Minneapolis and Oakland in this cooperative National Diet-Heart Study. A decade of hard work lies ahead to complete the overall job.

Perspective

This then has been a progress report, a report of significant advances by many investigators whose intensive efforts have been made possible by steadily increasing research support from the Heart Association and the National Heart Institute of the U.S. Public Health Service, that is, support from the American people via voluntary and tax dollars. But major research work remains to be done still, and with it a key question arises: What to do in the interim? What should medicine and public health at the "grass roots" do? What should the public generally do? Many signs point to the possibility of preventing heart attacks, but at the same time knowledge giving certainty is not yet in hand. And the mass field trials will certainly require the remainder of this decade, perhaps longer, before their results are available. Therefore the problem arises of an interim approach.

Two alternatives are possible. One might be called a more conservative alternative, and goes something like this: "All the new research information is very interesting and nice. It's good to see the research fellows making progress. We wish them luck. Admittedly, though, they haven't all the answers yet. In the meantime, therefore, we'll just wait and see." A corollary of this conservative wait-and-see approach is that no hope lies ahead for a major downturn in coronary disease incidence during the rest of the decade. No hope lies ahead particularly for men of high risk.

The alternative approach is: "The facts point very strongly in certain directions. They indicate the possibility of prevention. Moreover, and this is very important, they indicate that this possibility can be achieved pleasantly and—even more important – safely, because the procedures involved (nutritional, hygienic and pharmacologic) entail minimal risks. The nutritional and hygienic measures under medical supervision are essentially risk-free. The drugs for the control principally of hypertension and diabetes, when present, are drugs with which the medical profession now has a large experience; the risks with them are slight. Since the

TABLE XII
OVERALL CHANGE IN DAILY INTAKE OF FOOD GROUPS — TOTAL EXPERIENCE OF 99 PARTICIPANTS IN CORONARY PREVENTION EVALUATION PROGRAM

	CONTROL		TREATMENT	
FOOD GROUPS	CALORIES	PER CENT TOTAL CALORIES	CALORIES	PER CENT TOTAL CALORIES
Low fat dairy	44± 58.9*	2.1±2.9	134± 73.9	8.3±4.3
Medium & high fat dairy	202	7.8	26	1.5
Low fat beef, veal, lamb	32± 59.8	1.6±3.0	89± 69.0	5.6±4.4
Medium fat beef, veal, lamb	87±119.6	3.6±5.1	80± 72.5	4.8±4.1
High & very high fat beef, veal, lamb	309	12.6	105	6.1
Pork	169±178.0	6.6±6.2	56± 83.9	3.3±4.6
Poultry	81± 94.6	3.4±3.9	75± 51.8	4.7±3.2
Fish & sea food	33± 63.5	1.5±3.1	81± 67.9	5.2±4.3
Eggs	66± 5.0	2.8±2.1	8± 12.4	0.5±0.7
Bacon & lard	36± 53.3	1.4±2.0	10± 24.3	0.5±1.3
Butter & suet	116±103.5	4.5±3.7	15± 24.4	0.8±1.3
Margarine & hydrogenated oils	70± 78.6	2.8±3.0	24± 21.4	1.4±1.2
Oils & nuts	94± 88.8	3.9±3.6	124± 78.4	7.3±3.9
High fat baked goods	253±211.2	9.6±7.0	70± 89.4	3.8±4.2
Grains & starchy vegetables	433±139.2	18.3±5.4	409±113.7	25.1±5.7
Fruits & other vegetables	151± 79.8	6.6±3.9	205± 82.6	12.7±4.9
Sugar, candy, jellies, etc.	151±102.7	5.9±3.5	98± 65.7	5.7±3.3
Alcohol	136±206.8	5.2±7.5	67± 94.9	3.5±4.6

* Standard deviation of the mean.

possibility of prevention exists, since coronary disease takes such an epidemic toll, since the possibility of achieving prevention involves safe procedures, and since—without these new approaches—particularly the higher risk individuals do, in fact, have every likelihood of suffering markedly and without surcease from heart attack, it would seem that a sound interim approach (particularly for the higher risk individuals) would be to attempt to take advantage of the possibility of prevention. This is, in essence, the position taken by the American Heart Association in its Statements, "Dietary Fat and Its Relation to Heart Attacks and Strokes" and "Cigarette Smoking and Cardiovascular Diseases."

What does this mean for medicine and public health across the country? First, it would seem to mean active leadership and participation in the expanding effort to assess risk and detect persons with asymptomatic sub-clinical coronary disease, particularly through use of periodic examinations including biochemical tests, electrocardiograms, etc. Second, it would seem to mean active participation and leadership in the development of prevention programs.

What, then, is to be anticipated? What are the possibilities for the years ahead? There is reason for cautious optimism. From 1920 until the late 1940's, the total death rate from all diseases of the cardiovascular system increased for white men age 45-54 in the United States. In the late 1940's the death rate stopped rising for the first time in over 30 years. Then in the early 1950's it began to dip, and from 1950 to 1960 a phenomenon occurred that has been overlooked and unheralded—an actual decline, modest but definite, in mortality from the cardiovascular-renal diseases, for all sex-race groups Tables V-VIII). The toll is still great, but it may be that we are "over the hump."

In 1917, Chicago experienced 1216 deaths from diphtheria, many of them from diphtheritic heart disease. Who would have predicted then that in a few years this disease would be mastered and virtually eliminated.

In 1920, when rheumatic heart disease was a major scourge, who would have predicted that the death rate in children, teen agers and young adults would be cut so drastically that by 1959 it would fall to 10 per cent of the 1920 figure. Yet that is what has been achieved.

It is not unrealistic, unreasonable or unscientific to suggest that these are portents of what lies ahead as a result of the mounting effort to prevent premature sickness, disability and death from atherosclerotic coronary heart disease. It is not unrealistic, unreasonable or unscientific for medicine and public health to be bold—in keeping with the best traditions—to set big tasks and ambitious goals, for "there is a tide. . ."

Acknowledgments

It is a pleasure to acknowledge the support and cooperation forthcoming from Samuel L. Andelman, M.D., M.P.H., Commissioner of Health and Eric Oldberg, M.D., President, Chicago Board of Health. I want also to pay tribute to the staff of the Heart Disease Control Program, the Division of Adult Health and Aging, and the other divisions of

TABLE XIII

SERUM CHOLESTEROL LEVEL, BODY WEIGHT AND BLOOD PRESSURE CHANGES IN CORONARY PREVENTION EVALUATION PROGRAM PARTICIPANTS AT SUCCESSIVE TIME INTERVALS ON DIET

		Serum Cholesterol				Observed Weight / Desirable Weight			Blood Pressure		
Time on Diet (Weeks)	No. of Men	Control (mg./100 ml.)	On Treatment (mg./100 ml.)	Decrease (mg./100 ml.)	Decrease (%)	Control	On Treatment	Decrease	Control (mm. Hg)	On Treatment (mm. Hg)	Decrease (mm. Hg)
12 Weeks	69	276.6	233.5	43.1	15.6	1.263	1.169	0.094	134/88	126/82	8/6
29 Weeks	55	272.1	229.2	42.9	15.8	1.282	1.164	0.118	136/88	128/81	8/7
46 Weeks	44	273.8	229.8	44.0	16.1	1.265	1.145	0.120	134/86	128/81	6/5
80 Weeks	32	288.8	238.1	50.7	17.6	1.240	1.128	0.112	138/89	132/83	6/6
114 Weeks	9	323.1	260.4	62.7	19.4	1.250	1.136	0.114	136/88	125/81	11/7
All Men*	99	271.5	231.7	39.8	14.7	1.269	1.179	0.090	134/88	127/82	7/6

* Mean data on all men irrespective of time in study.

the Chicago Board of Health cooperating with us in research. I am pleased particularly to express appreciation to my senior research colleagues, who have contributed indispensably — David M. Berkson, M.D., Morton Epstein, Ph.D., Monte Levinson, M.D., Howard A. Lindberg, M.D., Joseph A. Mastropaolo, Ph.D., Louise Mojonnier, Ph.D., Yolanda Hall, M.Sc., Wilda Miller, M.P.H., Rahmi Soyugenc, M.Sc., and Rose Stamler, M.A. It is also a pleasure to acknowledge the cooperation of the staff of the Medical Department and the Executive Leadership of the Peoples Gas Light and Coke Company; Gilbert H. Collings, M.D., Medical Director and the Executive Leadership and the staff of the American Oil Company; Jacques M. Smith, M.D., W. C. Munnecke and the entire Executive Leadership of the Newspaper Division, Field Enterprises. We are also grateful to Paul Meier, Ph.D. of the Department of Statistics and the Biological Sciences Computation Center, University of Chicago.

We greatly appreciate the cooperation of our good colleagues Dr. T. R. Dawber, Dr. J. T. Doyle and Dr. E. C. Hammond of the Framingham, Albany and American Cancer Society studies respectively, who kindly granted us permission to reproduce material from their papers: (1) Kannel, W. B., Dawber, T. R., Kagan, A., Revotskie, N. and Stokes, J., III.: Factors of risk in the development of coronary heart disease—six-year follow-up experience. The Framingham Study, Ann. Int. Med., 55: 33, 1961. (2) Doyle, J. T., Dawber, T. R., Kannel, W. B., Heslin, A. S. and Kahn, H. A: Cigarette smoking and coronary heart disease. Combined experience of the Albany and Framingham Studies, New England J. Med., 266: 796, 1962. (3) Hammond, E. C.: Effects of smoking, Scientific American, 207: 39, 1962. We are also grateful to the Annals of Internal Medicine, the New England Journal of Medicine and the Scientific American, (reprinted with permission, copyright (c) 1962 by Scientific American, Inc. All rights reserved to reproduce these data.

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* In order to avoid a lengthy bibliography, the references here are limited to papers, monographs and books by the authors, in which extensive referencing is to be found.

THE PRESIDENT'S PAGE

1964 Election year, both state and national. A time of rhetoric and bombast, of charges and countercharges. A time when one party proclaims the true state of affairs, boasts of all its accomplishments in behalf of the people, and promises ever more and greater benefits if only it is kept in the driver's seat by so overwhelming a vote as to constitute a mandate; while the other bewails the complete distortion of facts presented the public, the unpublicized costs of the so-called accomplishments, and the impending disruption and bankruptcy of the country if it is not returned to power. Besides all the usual foreign and domestic policy questions add, this year, the complications produced by the decisions of the Supreme Court and various Federal tribunals ordering the redistricting for congressional seats and the reapportionment for all state legislatures—whether the states wish to or not. Then top it all off with the highly emotional and explosive issues of "states rights" and "civil rights" and we have a witches' brew that cannot do otherwise than leave us completely bewildered if not actually hanging on the ropes. From now until November 3rd promises to be an "interesting" time to say the least.

In all this turmoil what can we as physicians do? First of all we can certainly determine to vote and to induce our colleagues and families to vote. Failure to take the time to cast one's vote is a dereliction of duty in a democracy and an abrogation of one's responsibility. We can try to sift the wheat from the chaff—difficult though that may be. From the strictly medical point of view we should try to learn the position of candidates on medical and health care issues and support and vote for those who believe in the maintenance of freedom in the practice of medicine.

Here in Connecticut we already have an organization of our own whose purpose is to do just these things—the Connecticut Political Action Committee. COMPAC needs and deserves the support of every member of our Society. Even in its infancy it has demonstrated its possibilities in this regard. It can do a much better job if only we would really get behind it. It is rather disheartening to know that as of now *only* 25 per cent of our members have joined and are contributing to its work. Those of you who have not yet joined—think again. Here is an opportunity collectively to exert political influence which very few of us would spend the time or energy to do individually or could do as effectively. Join COMPAC today. COMPAC needs YOU. We need COMPAC.

RALPH L. GILMAN, M.D.
President

THIRTY-NINTH CONNECTICUT CLINICAL CONGRESS

of the

CONNECTICUT STATE MEDICAL SOCIETY

and the

YALE UNIVERSITY SCHOOL OF MEDICINE

Yale-New Haven Medical Center
Mary S. Harkness Memorial Auditorium
333 Cedar Street
New Haven, Connecticut

FRIDAY, SEPTEMBER 25, 1964

GENERAL INFORMATION

Registration:

Registration will begin at 9:00 A.M. The registration fee of $5.00 provides for admission to all sessions of the Congress.

Hospital residents, interns, and medical students will be admitted without charge, if a statement of their position, signed by an official of the hospital or school is presented at the registration desk.

Meeting Place:

All sessions will be held in the Mary S. Harkness Memorial Auditorium in the Sterling Hall of Medicine at the Yale-New Haven Medical Center. The entrance is at 333 Cedar Street. This comfortable auditorium will accommodate an audience of 450.

Telephone:

Telephone messages will be received at New Haven 562-1161, Extension 440.

Luncheon:

Luncheon for visiting physicians will be available in the Memorial Unit Cafeteria.

Parking:

There are pay parking areas for visitors adjacent to the Oak Street Connector between York Street and Park Street, behind the Memorial Unit, and also on Howard Avenue.

The Yale-New Haven Medical Center is about one-half mile west of the New Haven Green. It is easily reached from the Connecticut Turnpike (via Exit 47) or from Wilbur Cross (via Exit 61) or Merritt Parkway (via Exit 57)

Come for the Weekend—Attend the Clinical Congress on Friday, and the following activities on Saturday, September 26th—Surgical and Medical Grand Rounds at the Yale-New Haven Medical Center on Saturday morning and the University of Connecticut-Yale Football game on Saturday afternoon. Tickets may be obtained from the Yale Athletic Association, Yale Station, New Haven. Reserved Seats $4.00—General Admission $2.00.

Address inquiries to
Connecticut State Medical Society
160 St. Ronan Street
New Haven, Connecticut 06511

PROGRAM

FRIDAY, SEPTEMBER 25, 1964

MARY S. HARKNESS MEMORIAL AUDITORIUM

9:00 Registration (Coffee will be served until 9:30)

Morning Session

9:45 Welcome and Opening Remarks:

Ralph L. Gilman, Storrs, *President, Connecticut State Medical Society*

CORRECTABLE RENAL VASCULAR DISEASE

Marvin Lillian, *New Haven, presiding*

10:00 DIAGNOSIS OF CORRECTABLE RENAL VASCULAR DISEASE

John P. Merrill, *Boston; Associate Clinical Professor of Medicine, Harvard Medical School; Director, Cardiorenal Section, Peter Bent Brigham Hospital*

10:30 TREATMENT OF CORRECTABLE RENAL VASCULAR DISEASE

Michael E. DeBakey, *Houston, Texas; Professor and Chairman, Department of Surgery, Baylor University College of Medicine; Senior Attending Surgeon, Methodist Hospital*

11:00 PANEL DISCUSSION

Moderator: William Dock, *Brooklyn, New York; Professor of Medicine, State University of New York, Downstate Medical Center; Chief, Medical Service, Brooklyn V.A. Hospital*

Panelists: John P. Merrill—Michael E. DeBakey

Radiologist: Gilbert S. Melnick, *New Haven; Assistant Professor of Radiology, Yale University School of Medicine; Assistant Attending Radiologist, Grace-New Haven Community Hospital*

Urologist: Bernard Lytton, *New Haven; Assistant Professor of Urology; Yale University School of Medicine*

11:45 INTERMISSION

John C. Leonard, *Hartford, presiding*

12:00 CLINICAL PATHOLOGICAL CONFERENCE

Pathologist: David M. Spain, *Brooklyn, New York; Clinical Professor of Pathology, State University of New York, Downstate Medical Center; Pathologist, Brookdale Hospital Center*

Discussant: William Dock Radiologist: Gilbert S. Melnick

1:00 LUNCHEON

Afternoon Session

CORRECTABLE CEREBRAL VASCULAR DISEASE

Gilbert H. Glaser, *New Haven, presiding*

2:30 NATURAL HISTORY OF ATHEROSCLEROTIC CEREBRAL VASCULAR DISEASE

H. Houston Merritt, *New York City; Dean, Columbia University College of Physicians and Surgeons, and Professor of Neurology*

2:50 DIAGNOSIS OF CORRECTABLE CEREBRAL VASCULAR DISEASE

John Stirling Meyer, *Detroit, Michigan; Professor and Chairman, Department of Neurology, Wayne State University College of Medicine; Head of Department of Neurology, Harper and Receiving Hospitals*

3:10 MEDICAL TREATMENT OF CORRECTABLE CEREBRAL VASCULAR DISEASE

Joseph F. Fazekas, *Washington, D. C.; Associate Clinical Professor of Neurology, George Washington University School of Medicine; Attending in Neurology, V.A. Hospital*

3:30 SURGICAL TREATMENT OF CORRECTABLE CEREBRAL VASCULAR DISEASE

Charles Rob, *Rochester, New York; Chairman, Department of Surgery, University of Rochester School of Medicine; Surgeon-in-Chief, Strong Memorial Hospital*

3:50 PANEL DISCUSSION

Moderator: H. Houston Merritt

Panelists: John Stirling Meyer—Joseph F. Fazekas—Charles Rob

Radiologist: James H. Scatliff, *New Haven; Associate Professor of Radiology, Yale University School of Medicine; Attending Radiologist, Grace-New Haven Community Hospital*

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James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, July 15, 1964

I. Attendance

Present in addition to the Chairman, Dr. Martin, were: Drs. Cullen, Hess, O'Connor, Goldberg, Brandon, Davis, Weise, Sr., Gardner, Pitock, Grendon, Caplan, Shepard, Ayres, Ciccarelli, Seigle, Fabro, Egan, W. Martin, Spitz. Also present were: Mrs. Lindquist and Dr. Richards. Absent were: Drs. Gilman, Bradley, Grant, Phillips, Hughes, Rogol, Abbot, Hastings, Major.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of May 14, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Edmund J. Behan, New Haven (NHCMA)
John M. Freiheit, Wolcott (NHCMA)
John B. Griggs, Collinsville (HCMA) beginning 1965
Martin Heinemann, New Haven (NHCMA)
Charles L. Larkin, Waterbury (NHCMA)
Fernand Riendeau, Torrington (LCMA)
Michael S. Shea, New Haven (NHCMA) beginning 1965
Charles C. Wilson, New Haven (NHCMA)
S. Allison Rose, Stamford (FCMA) beginning 1965

CSMS Dues Exemptions

It was VOTED to grant exemption from payment of CSMS annual dues to the following, for the reasons and periods indicated:

Harold T. McDonald, Glenbrook (FCMA) Postgraduate Education 1964
Frank E. Dully, Jr., Shelton (FCMA) Military Service—half year for 1964
Raphael J. Toronto, Derby (NHCMA) Military Service
Nicholas M. Passarelli, New Haven (NHCMA) Postgraduate Education 1964
Kenneth G. Johnson, California (NHCMA) Military Service 1964
Ernest H. Ferrell, Jr., New Haven (NHCMA) for the duration of disability

Resignation—Committee On Health Careers

It was VOTED to accept, with regret, the resignation of Robert B. Pennington, Middletown, and to appoint William E. Gatlin, Middletown, to replace Dr. Pennington on this Committee.

Resignation—Ad Hoc Committee On Resolution No. 2

Having received notice that Lavius A. Robinson, Jr., Danielson, wishes to be replaced as a member

ADVANCE NOTICE

COMMITTEE SERVICE QUESTIONNAIRE

Each year the Councilors from the eight constituent county medical associations assume the responsibility of selecting members of the Society to participate in the various programs of the Society which are carried on through the activities of committees and related groups. In making these selections, it is of importance to choose physicians who are not only willing and able to serve but also who are known to have an interest in the work of committees and groups to which they may be assigned.

In 1961, a "Committee Service Questionnaire" was mailed to all members as a supplement to Connecticut Medicine and from the returns this office was able to furnish the Councilors with a compilation of those who had a desire to be nominated for committee service. In order to update this compilation, a second mailing of the questionnaire will be made as a supplement to the November issue of the Journal. Members are urged to be on the lookout for the supplement, to indicate on it their areas of special interest, and to return the completed form to 160 St. Ronan Street, New Haven.

of this Committee, it was VOTED to request Dr. Robinson to submit to the Council a formal letter of resignation.

Replacement—Public Relations Committee And Divisional Board

Having received notice of the death of Joseph L. Carwin, Stamford, Chairman of the Committee on State and National Public Relations and Chairman of the PR Divisional Board, it was VOTED to express a message of regret to Dr. Carwin's family.

It was further VOTED to appoint Luca E. H. Celentano, New Haven, to replace Dr. Carwin in both capacities for the remainder of the year, 1964-65.

Resignation—Committee On Aging

It was VOTED to accept the resignation of Ernest A. Bolt, Jr., Willimantic, as a member of this Committee.

Resignation—Committee On Rehabilitation

It was VOTED to accept the resignation of Leonard Flom, Fairfield, as a member of this Committee. Since Dr. Flom's membership on the Committee was by virtue of his being a member of the Committee on State Legislation, it was VOTED to appoint another member of the legislative committee, Brae Rafferty, Willimantic, to replace Dr. Flom on the Committee on Rehabilitation.

Resignations—Committee On Maternal Mortality And Morbidity

It was voted to make changes in the membership of this Committee as follows:

(a) Accept the resignation, with regret, of Benedict R. Harris, New Haven.

(b) Appoint Robert S. Gordon, New Haven, to replace Dr. Harris.

(c) Accept the resignation, with regret, of Donald W. Morrison, Manchester.

(d) Appoint Don A. Guinan, Manchester, to replace Dr. Morrison.

Request—Connecticut Nurses Association

Acting on a request of the CNA that the Society "send one or two representatives and (its) legal counsel" to a joint meeting with the CNA and the Connecticut Hospital Association, for the purpose of exploring "the dependent functions of nursing in the light of current and future complexities of patient care," it was VOTED to request the president of CSMS to appoint two representatives to participate in this exploratory meeting on September 23, 1964, but to refrain from imposing on legal counsel's time and services until the legal questions relating to the subject have been given definition.

Election Of Student Member

It was VOTED to elect to Student Membership Richard Wong, 39 Arcadia Road, Greenwich, Connecticut. Mr. Wong is a student at the Hahnemann School of Medicine, Class of 1967.

Date Of Next Meeting

It was VOTED that the Chairman select the date of the next meeting at his discretion, it being understood that no meeting would be called during the month of August unless necessary.

III. Old, New And Special Business

Life Membership And Dues Exemption

It was VOTED to request the Subcommittee to Study and Revise the Bylaws to study and report on the following:

(a) The criteria on which application of Life Membership may be made and aproved, with particular reference to the appropriate leniency or stringency of same.

(b) Definitions of the criteria on which Active Members may be exempted from the payment of CSMS annual membership dues.

Election—Committee On Preliminary Study Of Censorship Questions

Having received an appeal from a disciplinary decision of the Hartford County Medical Association from a member of that Association (provided for under the CSMS Bylaws, Article VII, Section 1, Paragraph 4), it was VOTED to elect a Committee on Preliminary Study of Censorship Questions to hear this appeal as follows:

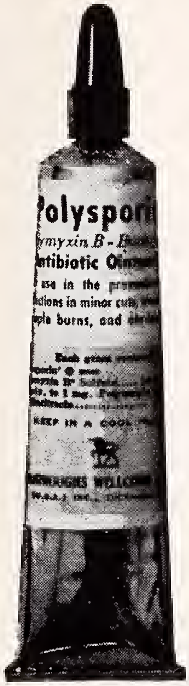
WCMA—Ralph L. Gilman, Storrs, Chairman
MCMA—John R. Egan, Old Saybrook, Vice-Chairman
TCMA—David S. Hastings, Stafford Springs
NHCMA—Waldo F. Martin, Milford
FCMA—E. Tremain Bradley, Norwalk
NLCMA—Nicholas T. Phillips, Norwich
HCMA—Kenneth F. Brandon, Hartford
LCMA—J. Alfred Fabro, Torrington

In hearing the HCMA member's appeal, it is understood that the HCMA representative on the Committee will not take part.

Request—Committee On Health Careers

On the recommendation of Bernard F. Mann, Jr., Chairman of this Committee, it was VOTED to authorize the disbursement of $200 from the general fund as the Society's contribution to a jointly-financed project to draw up specific plans for the formation of a proposed "Connecticut Health Careers Council." The Connecticut Hospital Association, the Connecticut Society of Pathologists, and a number of other voluntary health agencies in the state will make similar contribu-

in treating topical infections, no need to sensitize the patient



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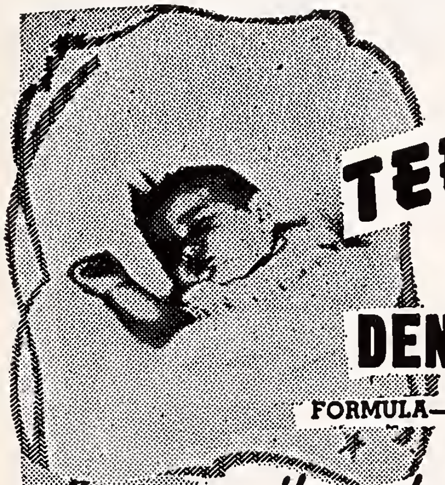

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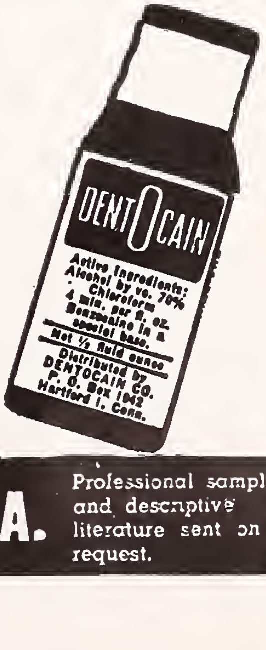

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tions to this project. Later, when plans are completed, each of the participating organizations will be asked to formally endorse and become members of the "Council."

Reports—Committee On Hospitals

(a) Acting on a request of the Committee on Hospitals that the Council "use whatever influence it can to expedite the realization of the pilot program of admitting selected clean gynecological patients in maternity units," it was VOTED to urge the Commissioner of Health to take all possible steps to expedite approval of this program by the Hospital Licensing Advisory Committee and, subsequently, the Public Health Council, in order that the program may be implemented at an early date. The purpose of this program is to relieve the rather critical shortage of gynecological beds which exists in many hospitals throughout the state.

(b) Considering a single report of the Committee which covered three unrelated matters, the Council acted as follows:

1. Regarding legislation being developed by the State Department of Health concerning the "abused (battered) child," it was VOTED to direct the president of the Society, Ralph L. Gilman, to offer the Commissioner of Health or his aides the assistance of the Society in drafting sound legislation to deal with this problem.
2. Regarding studies being made of the problem of financing hospital care of the premature or acutely ill newborn infant, presently being conducted by an Ad Hoc Committee under the direction of the State Health Department, it was VOTED to request a progress report on this subject from the two CSMS representatives on the Ad Hoc Committee, Samuel D. Rowley, Hartford, and Albert L. Larson, Hartford.
3. Regarding a report that a number of community hospitals throughout the state are considering the abolishment of "courtesy discounts" to physician staff members for hospital care services, it was VOTED to inform the Chairman of the Committee on Hospitals that the Council is not in sympathy with the philosophy of abolishing such courtesy to actively participating members of the staff nor in agreement with the reasons offered by the hospitals for contemplating such an action, and to request him to convey this opinion to the Council on Professional Practice of CHA.

Reports Of Delegates And Others

It was VOTED to accept as information the reports of delegates and representatives on their attendance at meetings of the following:

Connecticut State Dental Association—Ralph L. Gilman
Massachusetts Medical Society—Ralph L. Gilman
Connecticut Association of Medical Assistants—James R. Cullen
Congress on Medicine and Pharmacy—Bradford S. Colwell
Connecticut Pharmaceutical Association—Denis S. O'Connor

Other reports of special interest were received as follows:

(1) *Delegate to the Connecticut Hospital Association*:

Leonard M. Trifari reported that the Annual Meeting of CHA it was voted to consider reorienting the organization from a loosely-federated association of member hospitals to a more tightly-knit association in which the CHA governing body will have a greater influence in guiding statewide hospital policy in a number of key matters, including medical education, physician-hospital relations and third party purchasers of hospital care. It was further reported by the General Manager that the minutes of the CHA meeting indicate that the Association is giving serious thought to developing and operating a hospital planning council and that a proposal to accomplish this may be presented to a special meeting of the CHA in October.

Regarding this latter information, the CSMS Council VOTED to reaffirm to the CHA the interest of the Society in actively participating in any program or programs which deal with statewide hospital planning.

(2) *Report of the AMA Delegates*:

Drs. Weise, Cullen and Gardner gave summaries of the actions of the AMA House of Delegates on a number of matters brought before it, June 21-25, 1964. Official summaries of the San Francisco meeting will be published in *AMA News* and will also be reproduced in the next issue of *Connecticut Medicine*.

Report Of The Investment Committee

It was VOTED to accept the report of the Committee on Investments which indicated a modest but healthy growth of the invested funds.

Revised Bylaws—The Council Of New England State Medical Societies

Acting on the recommendation of the Delegates to the CNESMS that the Council "adopt" or "approve" the current bylaws of the N. E. Council (as revised on April 26, 1964), it was VOTED that, on the basis of information available, the CSMS Council not adopt or approve the CNESMS bylaws as submitted. The two main provisions on which clarification is to be sought are: (1) The status, rights, privileges, obligations and duties of each constituent state medical society as a "member" of the CNESMS; and (2) the status of CSMS officers, committee chairman and others as "members" of the CNESMS, and their authorization to vote at CNESMS meetings as "representatives and proxies" of the Connecticut State Medical Society.

Report—Chairman, Committee On Relative Value Study

Stewart P. Seigle, Hartford, recently appointed Chairman of the Committee on Relative Value Study, submitted a report to the Council concerning the work already completed on the Relative Value Study and the work which remains to be completed. It was VOTED to accept Dr. Seigle's report, and to authorize him to engage the services of a qualified statistician at the rate of $100 per day for a maximum of ten days for the purpose of obtaining professional counsel as to how best to proceed with the remainder of the Relative Value Study.

Report—Ad Hoc Committee On CSMS Staff And Committees

It was VOTED to accept a progress report of this Committee, filed by Orvan W. Hess, Chairman, concerning the Committee's continuing evaluation of the Society's public relations program, and to authorize Dr. Hess and his Committee to obtain professional public relations counsel, on a limited basis, to assist them in completing their evaluation of the activities of the PR Department.

1964-65 Medicare Agreement

Having received information that the Medicare authorities may be willing to remove a provision to cover the dependents of NATO military personnel from the 1964-65 Medicare agreement, it was VOTED to authorize the President of the Society and General Manager to approve the agreement as soon as notice is received of such action. In the event that notice to this effect is not received before the termination of the present period of extension of the 1963-64 agreement (August 31, 1964), the General Manager and the Chairman of the Medicare Committee are authorized to agree to a further extension of the previous agreement.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on July 15, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

OBSTETRICIAN-GYNECOLOGIST—Board Eligible, 30, 4 years training. Would like to locate in Southern Connecticut.

ORTHOPEDIST—Diplomate, American Board of Orthopaedic Surgery, 38, married, interested in private or established group practice.

UROLOGIST—Board Eligible, seeks to associate with medical group, or with an established urologist of Connecticut on salary basis and chance to partnership after one year. Connecticut license.

PLACEMENT OPPORTUNITIES

HARTFORD COUNTY — Internist's practice available, excellent location, abundant free parking.

HARTFORD COUNTY—Occupational Physician for state employee's clinic, located in Hartford. 35 hour week, 3 weeks vacation, up to 120 days sick leave, paid insurance program, social security and liberal retirement. Requires at least two years' general practice. Starting salary $11,640 going to $12,380 at end of first year, then advancing $540 annually to maximum of $15,080. Reply directly to B. Dearington, State Department of Health, State Office Building, Hartford, Connecticut.

HARTFORD COUNTY—Wanted senior physician for Veteran's Home and Hospital. License to practice medicine and surgery in Connecticut. Special training in Internal Medicine especially desired.

NEW LONDON COUNTY—Physician needed in fast-growing Town of Ledyard: 10,000 people; no resident physician. Space available in new professional building next to Town Hall, School, Post Office, etc.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST, RONAN STREET, NEW HAVEN.

OBITUARY

Louis F. Wheatley, M.D.
1876 - 1964

Dr. Wheatley was born in Westboro, Massachusetts, December 16, 1876, moving later to Brookfield, Vermont and then to Meriden, Connecticut. He graduated from Meriden High School in 1893, University of Vermont in 1898, and Tufts Medical School in Boston in 1903. He interned at Cambridge Massachusetts Hospital and did graduate work at Boston Floating Hospital.

In 1906 he started practice of medicine in Meriden where he was Health Officer 1910-1917. He then entered the U. S. Army as a lieutenant at the Military School of Roentgenology in New York City and was transferred to the U. S. General Hospital in Denver, Colorado, where he developed the X-ray Department. After his discharge in 1919 from the Army, he came to New Haven as director of the X-ray Department at Grace-New Haven Community Hospital which he served until 1938.

He then opened on office for the private practice of roentgenology at 61 Trumbull Street. He retired in 1950 at age 74 and spent his summers at the family home in Brookfield, Vermont and winters in Orange City, Florida.

He was a member of the staff at Meriden Hospital and served as president of the Meriden Medical Society. He was a member of the New Haven County Medical Association and the Connecticut State Medical Society where he had been president of the Section on Radiology. He was also a member of the A.M.A. and a diplomate of the American Board of Radiology.

Dr. Wheatley was a charter member of the University Glee Club of New Haven; a Deacon of United Church on the Green where he was chairman of the Music Committee for many years, and a long time member of the Kiwanis Club of New Haven. He was a member of the New Haven Country Club where golf was his chief hobby after his singing and music activities. After his retirement, he continued his golf, choral and church singing, both in Vermont and in Florida.

He died July 5, 1964 in Gifford Memorial Hospital, Randolph, Vermont, following an exploratory laparotomy for inoperable carcinoma. He was buried in Meriden, Connecticut, on July 7, 1964.

Dr. Wheatley married Leila Illingsworth in Meriden in 1907 who predeceased him in 1956. He leaves two daughters, Mrs. Donald Brooks of Woodbridge, Mrs. George Bladworth of Marbelhead, Massachusetts, and a son, John Wheatley of Mt. Carmel, Connecticut, nine grandchildren and ten great-grandchildren.

Ralph W. Nichols, m.d.

In Memoriam

Cognetta, James J. — Stamford; University of Vermont Medical School, 1936. Dr. Cognetta was a general practitioner in Stamford for 27 years. He was on the attending staffs of the Stamford and St. Joseph's Hospitals. Dr. Cognetta was a member of the Stamford Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of General Practice. Dr. Cognetta died August 7, at the age of 54.

Dunne, Edward P.—Unionville; University of Maryland College of Physicians and Surgeons, 1916. Dr. Dunne was a general practitioner in the Farmington Valley for 45 years. He was honored many times for service to the community and dedicated to the medical profession. Dr. Dunne was a member of the American Medical Association, the Connecticut State Medical Society, the Hartford County Medical Association, and many civic organizations. Dr. Dunne died July 28, at the age of 76.

Letters To The Editor

William R. Richards, M.D.
Business Manager
Connecticut Medicine
160 St. Ronan Street
New Haven 11, Connecticut

Dear Bill:

As editor of *Massachusetts Physician,* I receive most of the state medical journals on an exchange basis. While I do go over all of them, the one journal to which I devote special attention is *Connecticut Medicine.*

Your latest issue (July 1964) is really outstanding. From the guest editorial by Dr. Max Caplan, the several editorials by Dr. Louis H. Nahum (and it is a matter of amazement that Dr. Nahum can contribute so many carefully thought out articles), the articles by Dr. McCawley and Dr. Foote and the others, to the very last page, the whole issue—that part that is devoted to quackery—deserves publication in a lay magazine of mass circulation.

The medical profession is more or less acquainted with the facts on quackery, but the public at large is not. I hope the issue will be called to the attention of the editors of such publications as *Life, Saturday Evening Post* or *Look.*

My congratulations to Dr. Caplan, Dr. Nahum and the entire staff of *Connecticut Medicine.*

Kind regards.

Cordially,
Carl Bearse, M.D., Editor

Boston, Mass.

To the Editor:

Because many of my medical colleagues have been asking me why I recently resigned from the Board of Directors of CMS and also as a CMS Participating Physician, I submit this letter of explanation for the benefit of other members of the Society who may be interested in the reasons for my decision.

First, let me say that I have always held Connecticut Medical Service, Inc. in high esteem as an instrument for public service by the Connecticut medical profession and, as one of many Participating Physicians, have taken great pride in personally contributing to its rapid ascendancy to a superior rating among the Blue Shield plans of the nation. I considered that the State Medical Society had made a wise decision to sponsor the plan in 1948, and used good judgment in making an interest-free loan of $5,000 to help get it started.

It is not surprising, therefore, that when I was named by the Society in 1963 to serve as a Director of CMS, I felt greatly honored to be asked and agreed enthusiastically to accept nomination by the Council. Even when the CMS Corporators bluntly refused to ratify my appointment, and later accepted me reluctantly and only by order of the courts, I still believed that it might be possible for me to make a worthwhile contribution to good medical care in Connecticut by carrying out the duties and responsibilities of a member of the CMS Board.

When I was finally seated as a Director, with half of my two-year term already expired, I was not unmindful of the fact that neither I nor anyone else had ever been told why I had not been considered acceptable for the post in the first place. I determined, however, not to let this unwarranted slur on my professional reputation disturb me greatly because I was firm in the belief that my qualifications for the office could not be challenged. As a staff member in good standing at five approved Connecticut hospitals; as Chief of Medicine at one of them; as a Trustee of a national gastroenterological society; as a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine; as an AMA Delegate; as an Assistant Clinical Professor at the Yale School of Medicine; and so on, I knew I did not have to apologize for my credentials. Whatever may have been in the minds of others, my conscience was clear.

Holding to the opinion that the phrase "Sponsored by the Connecticut State Medical Society" was still meaningful, and that our members—through the Society—were entitled to have an equal voice in the CMS plan, I attended every board meeting to which I was invited during the Spring of 1964. Since I had been denied my rightful place on the Board for nearly a year I spent a great deal of time trying to familiarize myself with the proceedings of the Corporation during the period of my exclusion, and attempted to participate constructively in the meetings currently being held. As time went on, however, it became apparent to me that mine was likely to be a "voice in the wilderness" since on almost every issue concerning the disputed relationships between CMS and the Society I found myself to be in a definitely minority position. This experience was rather frustrating, to say the least.

When the House of Delegates (April 28, 1964) confirmed that sponsorship of CMS by the Society no longer existed, my first reaction was to resign from my directorship immediately. But I decided not to do so because I still hoped that the more discerning minds on the Board would come to realize that this severing of relations would prove to be disadvantageous to all concerned if allowed to persist.

However, I found that during the two months following the action of the Delegates a majority of Corporators not only failed to take the least cognizance of the serious nature of the breach which had occurred but also were engaged in making plans to operate CMS with complete disregard of the known policies of the State Medical Society.

Faced with this situation, I concluded that I could no longer in good conscience continue my membership on the CMS Board and I submitted my resignation. At the same time, and for the same reasons, I also resigned as a CMS Participating Physician. I took both these actions because of my firm conviction that physicians and their patients can benefit

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180TH SEMI-ANNUAL COUNTY ASSOCIATION MEETINGS

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September 30—Fairfield County
October 1—New London County
October 13—Litchfield County
October 15—Windham County
October 20—Tolland County
October 29—New Haven County

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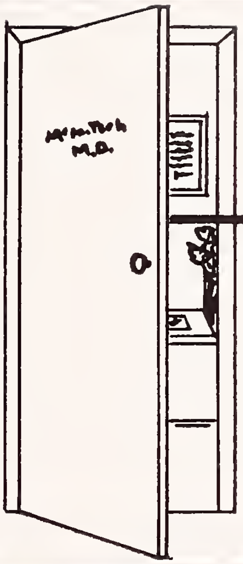

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greatly from such a prepayment plan but *only* if they work together as equal partners—a condition which does not prevail in CMS today.

It is possible that some members of the Society will not come to share my views or reach the same decisions I have, and that is certainly their privilege. However, being acquainted with the circumstances which have led our confreres in so many other lands down the road to complete control by agencies outside their established medical organizations, I cannot help but urge every physician in Connecticut to seriously consider whether guaranteed payments or his professional freedom will, in the long run, prove of greater importance to himself and of greater benefit to his patients. In my own mind the choice is clear but, in any event, one thing is certain—we can't have it both ways.

Max Caplan, m.d.

Meriden, Conn.

To The Editor:

I am enclosing a short article entitled "Physician Take a Look at Thyself" for your consideration. I believe this short article to be of importance for the future of our cherished profession.

Physician Take A Look At Thyself

"*The British Medical Journal* recently reported that in Great Britain the suicide rate among M.D.'s is twice the rate in the rest of the male population. From similar reports from other countries, including the United States, it results that the high suicide frequency among physicians is not peculiar to England alone. Six per cent of all doctors' deaths under the age of 65 are from suicide; the same as from cancer of the lungs.

One causative factor of the high suicide rate among M.D.'s given is "doctor's inhumanity to doctor." That a physician could be inhuman altogether is already quite repulsive, that such inhumanity be directed against his own colleagues is simply revolting.

An M.D.'s characteristic should be devotion, sympathy, understanding, readiness to help at all times, all things which negate the meaning of inhumanity. How then can physicians be inhuman, and to their own colleagues at that?

The answer to that question seems to lie in the fact that the modern M.D. is ceasing to be the old fashioned physician in the strict Hippocratic meaning. Medicine is quickly becoming just another profession more and more compartmentalized in many different and increasingly restricted specialties. Many medical schools have already ceased to administer the Hippocratic oath at the graduation exercises. Is it surprising that many of those who are supposed to keep others from committing suicide are getting discouraged themselves, begin to ask themselves the question "what's the use?" and finally decide to give up the fight?

Is it not time for the medical profession to take a look at itself, perform a good introspection and root out all the weeds which invaded the medical soul in these years of great technical progress?"

Yours very truly,
Marcel Thau, M.D.

Hartford, Conn.

Doctor's Office

James J. Bingham, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 46 Mt. Pleasant Road, Newtown.

Joseph G. Buchman, M.D., announces the opening of an office for the practice of internal medicine and cardiology at 20 Main Street, Ridgefield.

Joseph C. Carpentieri, M.D., announces the opening of an office for the practice of ophthalmology at 21 Woodland Street, Hartford.

Paul R. Fleisher, M.D., announces the opening of an office for the practice of urology at 435 Montauk Avenue, New London.

Jay M. Hughes, M.D., announces the opening of an office for the practice of internal medicine at 56 Hayes Street, Manchester.

W. Frederick Lahvis, M.D., announces the opening of an office for the general practice of medicine at 60 Bridge Street, New Milford.

Warren Zeph Lane, M.D., and Henry Davis Minot, M.D., announce their association with Marshall Franklin, M.D., in the practice of medicine at 1116 Summer Street, Stamford. They are cooperating in forming a medical group to be called Thoracic Associates, specializing in diseases of the chest.

Robert J. Manjoney, M.D., announces the opening of a second office for the practice of obstetrics and gynecology on Monroe Turnpike, Rt. 11, Monroe.

Carlos Peralta, M.D., announces the opening of an office for the practice of general surgery at 881 Lafayette Street, Bridgeport.

Edward A. Post, M.D., announces the removal of his office for the practice of urology to 1389 West Main Street, Waterbury.

Louis Schlessel, M.D., announces the opening of an office for the practice of eye, ear, nose, and throat at 2331 Whitney Avenue, Hamden.

Jay D. Smith, M.D., announces the opening of an office for the practice of general medicine at 10 Princeton Street, West Hartford.

Barry M. Winters, M.D., announces the opening of an office for the general practice of medicine at 56 Broad Street, Milford.

Joseph G. Wihbey, M.D., announces the opening of an office for the practice of general surgery at 452 Meriden Road, Waterbury.

Alvin Wolfson, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 2044 Bridgeport Avenue, Milford.

NEPHROPATHIES SAID TO BE ASSOCIATED WITH ANALGESIC ABUSE

Over the past several years there have appeared in medical literature, particularly in Europe, reports of toxicities associated with excessive use of analgesics and analgesic mixtures containing drugs such as aspirin, phenacetin, acetaminophen, antipyrine, aminopyrine, caffeine, barbiturates and other sedatives. Because of this, the medical and research staffs of Burroughs Wellcome & Co. have conducted in their own research laboratories and in collaboration with pharmacologists, nephrologists, pathologists, hematologists, microbiologists in other institutions and medical schools, comprehensive animal and human studies to elicit more information concerning the mechanism of action, the usefulness and the extent of untoward effects of various analgesics.

Evidence Does Not Prove "Phenacetin" is the Causal Agent

The first report of possible toxic effects from long-term drug abuse came from Switzerland in 1953 where there was observed what appeared to be an increase in the incidence of chronic interstitial nephritis. The patients involved had taken a wide variety of drugs, including antibiotics and sulfas, and had also ingested over many years large quantities of analgesic mixtures. In this first report, one of the analgesic mixtures most commonly used to excess was a mixture containing 150 mg. isopropylantipyrine, 250 mg. phenacetin, 50 mg. 3,3,-diethyl-2,-4-dioxo-tetrahydro-pyridine (a sedative) and 50 mg. caffeine. Despite the complexity and excessive overuse of the mixture, plus the fact that patients were consuming various other drugs as well, "phenacetin" was arbitrarily designated as the nephrotoxic agent.

Other reports appeared, and with the passage of time the lesion most commonly associated with excessive use of analgesic mixtures was a chronic pyelonephritis accompanied in some instances by papillary necrosis. In these later reports other types of analgesic-sedative-stimulant mixtures were implicated. A formula often abused in Sweden contained 500 mg. antipyrine, 500 mg. phenacetin and 100 mg. caffeine; one in Australia contained approximately 7.8 gr. aspirin, 2.6 gr. phenacetin and 2.6 gr. caffeine citrate. It should also be noted that, according to the reports, persons abusing the analgesic mixtures in Switzerland, Sweden, Australia and elsewhere often took 10, 20 or more of the analgesic powders or tablets each day and for long periods of time. This is a lot of aspirin, antipyrine, phenacetin and caffeine to be ingested daily.

Though there has been this tendency to associate "phenacetin" arbitrarily with untoward effects of analgesic abuse, evidence available does not prove phenacetin as such is the specific causal agent.

←Continued

Abuse in Europe, Australia and the United States

Apparently a great many more cases of analgesic abuse have been reported in such countries as Switzerland, Sweden, Denmark and Australia than in the United States. The "drug mixtures" commonly used and "abused" in these overseas areas have contained larger amounts of aspirin, caffeine, antipyrine, aminopyrine and other such drugs than would normally be found in formulas in the United States. For example, although it is rarely used here, extremely large amounts, 5 Gm. (75 grains) or more, of antipyrine or aminopyrine were consumed daily by persons in Europe.

Our extensive investigation of the literature and discussions with men knowledgeable in various ways about the problems of nephropathy lead us to believe that in the U.S.A. the number of cases of renal disease in which the abuse of analgesics may be implicated is relatively very small.

Analgesic Abuse - The Crux of the Problem

Based on the reports examined, there seems to be no sound evidence that phenacetin as such is specifically the cause of the cases of nephrotoxicity which have been ascribed to it. In the cases of toxicity reported, individuals consumed indiscriminately other analgesic drugs and analgesic mixtures and also the other drugs mentioned, such as stimulants and sedatives, in extraordinarily excessive amounts, chronically and for long periods of time. This would appear to be the crux of the matter.

Other Factors May Be Involved

Most of the clinical reports of nephrotoxicity assumed to be associated with analgesic abuse have resulted from retrospective studies. Findings from retrospective research may often be of value, but since one is dealing with a disease (pyelonephritis) of relatively high incidence (3% to 6%) and with drugs that are very widely used, it is possible that circumstantial evidence could lead to false or tenuous conclusions, both as to the causative factor and the magnitude of the problem.

A most important factor to be carefully considered is that many of the patients involved had bacteriurias and pyelonephritis, conditions that undoubtedly would have caused them to use analgesics for the relief of associated headache and "low-back" pain.

Also of significance is that a study of case reports shows that many of the patients with adverse reactions attributed to analgesic abuse had a multiplicity of functional and psychic disorders and had been using excessively a wide variety of drugs. These included not only analgesic mixtures but also sedatives, stimulants, antibiotics, sulfas and other antibacterial agents.

Acetic-4-Chloranilid - An Impurity in Phenacetin

Phenacetin produced in the U.S.A. is virtually free of acetic-4-chloranilid, a contaminant present in phenacetin produced in some other countries. The British Pharmacopoeia allows up to 0.17%, Denmark allows up to 0.35%. Burroughs Wellcome & Co. has a limit of 0.01%, and in most instances there is so little present the amounts are not detectable by the sensitive tests used. So far it is not known if acetic-4-chloranilid is a factor in the toxicities reported.

Studies of Toxicity, Action and Metabolic Fate of Analgesics

Nephrotoxicity of chemical agents is usually detected in experimental animals, but administration of high doses of analgesic drugs such as aspirin, phenacetin and acetaminophen, alone or in mixtures, to laboratory animals has not provided conclusive evidence of specific renal toxicity. Extensive studies with animals have been done and are continuing.

There has also been undertaken comprehensive research on the metabolic fate of phenacetin, acetaminophen and related compounds in both animals and man, and it is hoped that eventually this work will provide useful information.

So far the effect of excessively high doses of analgesic drugs and mixtures given to laboratory animals for long periods would appear to be one of lowering resistance to bacterial infection. It is probable that many drugs ingested excessively could result in a lowered resistance to infection.

Aspirin and Phenacetin - Analgesics of Low Toxicity

It is our feeling that aspirin and phenacetin, both of which have been used extensively for over 60 years, are:

Effective, useful analgesics and antipyretics.
Drugs of low toxicity.
Unlikely to cause harmful effects when used sensibly in doses as recommended.

Why the 'Empirin' Compound Formula?

Based on present knowledge, we believe it is unlikely that any replacement for aspirin or phenacetin could, in the long run, prove to have significantly lower toxicity. *We also believe that satisfactory analgesia with fewer possible side-effects is achieved when aspirin and phenacetin are combined in smaller amounts than would normally be used if each were taken separately.* This is the pharmacologic basis for combining the two analgesic drugs, aspirin and phenacetin, in 'Empirin' Compound.

In respect to this, it is interesting to note what Goodman and Gilman have to say on page 313 of their book, "The Pharmacological Basis of Therapeutics":

> "As emphasized for barbiturates and again for salicylates, a smoother and more efficient analgesic action may be obtained by prescribing a mixture of two or three analgesic chemicals. These should be selected from different classes of drugs and the dose of each reduced to one half or less. This represents one of the few valid uses of drug combinations. The possibility of untoward reactions is also reduced because the toxic effects of the salicylates, pyrazolon, and para-aminophenol derivatives differ somewhat from each other."

When used in moderate doses, as recommended, 'Empirin' Compound and its combinations with Codeine Phosphate are reliable, effective and safe analgesics for the relief of pain and headache. They have a long record of usefulness and safety.

—*Continued*

Conclusion and a Recommendation

Though authorities have stated there is no public health problem when analgesics are used sensibly, Burroughs Wellcome & Co. will continue to conduct and collaborate in further animal and human studies.

We also recommend that all members of the health team and the public be alert to the fact that harmful effects can result from misusing all drugs, including analgesics.

To discourage abuse, labeling of 'Empirin' Compound has included for many years a statement that adults should not take more than 6 tablets in a 24-hour period. To further minimize possible misuse, we have added a statement that if pain persists or recurs frequently, the patient should consult his doctor. There is also a warning on the label that 'Empirin' Compound, like all medicines, should be kept out of the reach of children.

* * *

A Review and Bibliography Available on Request

We have investigated in depth the reports of nephropathies alleged to be associated with the abuse of analgesic drugs and analgesic drug combinations. As a result of these investigations and discussions with many physicians and investigators expert in renal physiology and renal diseases, a Review and Comprehensive Bibliography on Analgesic Abuse has been prepared. We hope the information in it will help bring this complex subject into better balance and perspective. A copy is available on request.

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BOOK REVIEWS

MEDICAL PHARMACOLOGY: PRINCIPLES AND CONCEPTS, Andres Goth, 2nd Edition, 585 pages, 20 tables, 59 figures, C. V. Mosby Co., St. Louis, 1964. $11.75.

Reviewed by: LOUIS H. NAHUM

The first edition of this book came out in 1961 and the progress has been so rapid that this 2nd edition became mandatory. Many drugs now widely used were not known and many concepts widely held were not readily understood. Since the thalidomide diaster we have become much more conscious of toxicity of drugs as well as their activity. Because large numbers of drugs are used in practice, they need to be intelligently understood for safety, mode of action, side effects, toxicity and metabolism. This is clinical pharmacolologic knowledge, difficult to ferret out of a large comprehensive textbook and not entirely made clear in a book just on drug therapy.

The in-between book is this one, and it will be a source of illumination and intellectual stimulation to students and practicing physicians to whom it is directed. We are all being influenced in our drug selection by detail men and advertising pages. A good understanding of the principles can provide the physician with a critical attitude and ability to evaluate rationally the claims made for many new drug preparations.

Many original chapters were enlarged to include and evaluate practically all of the recently introduced drugs such as newer antihypertensive agents, newer penicillins, diuretics and many others. Here we find the mode of action of sympathomimetic drugs, release and metabolism of catecholamines, beta adrenergic blocking agents, treatment of drug addiction, how to select an appropriate antibiotic. For the students better insight, there is present concepts of drug metabolism, passage of drugs across body membranes, recogniion of the important role in regulation of bodily functions by "internal drugs" such as hormones, acetyl-choline, nor-epinephrin, histamine, serotonin, heparin.

The author is acutely aware that results of drugs obtained by animal experiments must then be validated by observations in man and what we learn here is activity in man. While it is true that development and elucidation of basic mechanisms of drug action will continue to originate from animal experiments, they must then be tested by the clinical pharmacologist in man and the resulting knowledge is what we find in this book.

Even though the book is excellent for the practicing physician in his interpretation of the mechanisms and action of drugs, he will also receive a "second education" in the way in which physiologic and biochemical processes can be influenced by drugs. It is interesting that a student suggested many changes in style and organization so that the book is written from the student's and physician's point of view. The book is well printed and the publishers have done an excellent job in reproducing the tables and figures. It will prove to be a source of pleasure and sitisfaction to anyone who uses drugs, be he surgeon, physician, anesthetist or student.

CHRISTOPHER'S TEXTBOOK OF SURGERY, Loyal Davis, M.D., Editor. W. B. Saunders Company, Philadelphia and London, June 16, 1964, 1,481 pp., illustrations: 1341 on 744 figures. $18.50.

Reviewed by: IRA S. GOLDENBERG

Surgical diagnostic and therapeutic techniques have been advancing at a dizzying pace during the past decade and a problem almost as big as achieving such advances is reporting progress to the medical reader before the material becomes outmoded. Perusal of current medical periodicals certainly is one way, probably the best way, to keep abreast of the times, but many busy physicians with restricted time to read have difficulty covering, or even choosing, among, the multitudinous journals of the day. Thus, a comprehensive textbook surveying a given field is an obvious answer to the problem of information dissemination, but detail must suffer or the book becomes massive and impractical.

The author has accomplished the difficult task in this text of keeping its size reasonable. Dr. Davis utilizes group editorial participation to do a big job with relative speed and ease and in this way has engineered four editions of Christopher's classic textbook. In fact, it should probably soon be titled "Davis' Textbook" since the solo editions of the late Dr. Christopher and the present volume are as closely related as the Wright Brothers' plane to a jet.

The group of learned surgeons who have contributed to this 8th edition are outstanding academicians of our era and their handling of the diverse aspects of surgical practice in the 1960's is complete, interesting and certainly educational. This volume is particularly for the bookshelf of the medical student and the house officer or the practitioner who requires information about surgical problems presented succinctly and intelligibly. It is recommended especially for the generalist needing insight into surgical management burdened only with such details of techniques as are necessary to gain an overall picture of the subject at hand.

CURRENT DIAGNOSIS AND TREATMENT, Henry Brainerd, Sheldon Margen, Milton J. Chatton and 30 Associate Authors, 870 pages, Lange 1964. Price $9.50.

Reviewed by: LOUIS H. NAHUM

This book is a first class effort to present diagnosis and treatment of disease. It is a most valuable desk reference on the most widely accepted techniques currently available for diagnosis and treatment. It is a handbook not a text book and is more up-to-date than text books because of the annual revisions which come out each January. There is more in it than just internal medicine. There are some specialties like skin, eye, ear, nose, throat. There is an excellent coverage of neuropsychiatric disorders and sound approaches to the management of such patients.

Inside the front cover are normal values in hematology including blood chemical constituents. Inside the back cover are liver function tests, renal function tests and miscellaneous

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normal values. There are desirable weight tables, chemical analyses of blood and body fluids, a much needed glossary of genetic terms. Then drugs recently withdrawn, drugs recently introduced and unestablished drugs. A glance at these lists will quickly orient the physician.

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Every physician will gain security in his management of patient if he has this book at his desk. The book is an excellent effort and warmly recommended.

MODERN TREATMENT, Vol. I, No. 1, Treatment of Renal Disease, Edited by E. Lovell Becker, M.D., Treatment of Thyroid Disease, Edited by Edward A. Carr, Jr., M.D., Hoeber, New York, N. Y. A new bimonthly book series. By subscription only: 6 books a year. 1200 pp. per year, $16.00 per year.

Reviewed by: WILLIAM F. ECKHARDT, JR.

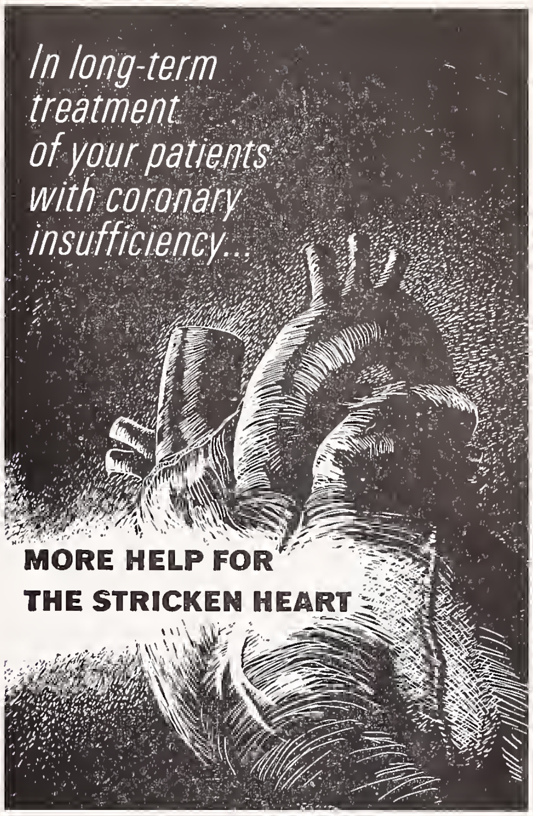
According to the publisher, *Modern Treatment* has been created to "keep the physician abreast of the dramatically advancing front of medical therapy." If subsequent volumes, to be published bimonthly, meet the high standards of the initial offering, *Modern Treatment* will be successful in at least partly fulfilling its purpose.

A guest editor, expert in a field of medicine, arranges the topics and coverage of his symposium. The contributors to each symposium are well-known experts who have written extensively about their subjects. The editors have wisely not restricted their contributors to a mere discussion of therapy, despite the name of the monograph. Each paper can stand alone as relatively complete, albeit brief, discussion of etiology, pathophysiology, as well as treatment of the topic. Some of the topics covered in the first number devoted to Renal and Thyroid Disease, are the treatment of acute renal insufficiency, chronic renal failure, acute glomerulonephritis and pyelonephritis, hypothyroidism in infancy and adulthood, thyroiditis which is completely reviewed, and malignant disease of the thyroid.

Future issues will discuss treatment of the Anemias, Liver Disease, Epilepsy, Cardiac arrhythmias, Pulmonary diseases, and Infectious diseases.

The major problem with this journal, as with other review publications, is the time it takes for the review to be published from the time of its conception. None of the reviews list references to papers published later than 1962. In most instances, this lack of completeness is not vital but a few of the reviews such as the discussion of "Peritoneal Dialysis and Hemodialysis" are not up-to-date. In fairness, Schreiner's "Treatment of Chronic Renal Failure" and Degroot's Therapy of Thyrotoxicosis are superb and are well worth the cost of the entire series.

Most physicians will find *Modern Treatment* helpful and authoritative and it might find a place as a substitute for the replacement of textbooks of medicine which are totally out of date on publication. For the sophisticated physician, *Modern Treatment* will not replace careful reading of his medical journals and attendance at medical meetings.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Planning Urged For Health Care Of U.S. Athletes At Olympics

A plea for appropriate planning for the health care needs of U.S. Olympic athletes competing in Tokyo in October was made in an editorial in the current Journal of the American Medical Association.

The editorial cited the problems at previous Olympic and Pan American Games and urged more advance medical consultation for this year's event.

The AMA Committee on the Medical Aspects of Sports has been unsuccessful to date in encouraging broader utilization of the existing U.S. Olympic Subcommittee on Medical Services and the appointment of an appropriate physician to the subcommittee, the editorial pointed out.

"At the moment, the [AMA] committee is not aware that medical consultation is being sought concerning measures to counteract environmental health problems, supervision of the athletes' diets, and other training and conditioning procedures," it said.

"Nor is the committee aware that any plans are being made for the health orientation of those selected to represent the United States.

"It is hoped that those in charge of the arrangements for the U.S. Olympic Team, recognizing the diminishing time available for effective planning, will become actively engaged in appropriate medical consultation."

The United States will probably send more than 400 men and women to Tokyo for the games, the editorial pointed out.

"The transportation of all these athletes to Japan and their accommodation during the team's stay create considerable problems in logistics and medical care," it said. "While striving for peak performance, our men and women will be exposed to different environmental conditions, unfamiliar food, water of a different quality, endemic [prevalent] diseases, and a new pattern of living."

Long-term health planning for previous games has "left something to be desired," the editorial said.

The two team physicians and the athletic trainers who made the trips to Rome in 1960 and Brazil in 1962 were well qualified but too few in number to satisfy the needs of the U.S. teams, the editorial said, adding:

"They were not involved in comprehensive planning and did not have the time at the site of competition to overcome the resulting difficulties."

Several hundred cases of dysentery occurred among U.S. team members in Rome and more than 100 in Brazil, the editorial continued.

"American food was supplied in Rome, but in quantities so bountiful that some contestants ate themselves out of competitive condition," it said.

"In 1960, the members of the track and field team were taken through a rapid series of exhibition meets in cold and rainy weather in Europe and then brought into the searing heat of Rome only a few days before the games. Competitors were encouraged to enjoy sight-seeing and the local hospitality before their events had been completed."

Tokyo will present problems of perhaps greater difficulty than on any previous Olympic trip, according to the editorial.

"The effects of errors and omissions in the provision for proper health supervision are not always evident, but it is clear that appropriate planning will minimize potential problems and help to assure the high level of performance necessary for the expected stiff competition," the editorial concluded.

AMA Committee Urges Sports For Girls

The American Medical Association Committee on the Medical Aspects of Sports urged greater development of sports opportunities for more girls and women in the United States.

The committee expressed concern about the inadequate provision for physical activity for a large proportion of the nation's feminine population.

Whether from culturally-imposed restrictions, untenable physiological taboos, or from disproportionate allotment of time, facilities, and leadership, many are not receiving the desired experiences from suitable and regular physical activity, the committee said.

"The health benefits of wholesome exercise are now well substantiated, and are just as pertinant to the female as to the male. The woman who maintains a high level of health and fitness can meet family or career responsibilities more effectively, and can pursue avocational interests more enjoyably. Also, and not unimportant, participation in healthful physical recreation is now accepted, rightfully, as contributing to the feminine image instead of detracting from it."

It is "imperative," the committee continued, that all girls be reached and involved in sports programs commensurate with their respective capacities and interests.

Hot Weather Training

The American Medical Association's Committee on the Medical Aspects of Sports once again has issued its annual pre-fall admonition regarding early season football practice in hot weather.

Special precautions should be observed to safeguard the health of college and high school athletes at the outset of the season, especially when the practice periods are conducted in very warm and highly humid weather.

The tens of thousands of youths who will shortly be trying to make the school teams all over the nation will be subject to heat exhaustion or heat stroke if care is not observed. Heat exhaustion follows depletion of salt and water due to excessive sweating. In heat stroke, the body overheats due to lack of sweating.

The old idea that water should be withheld from athletes during workouts has long since been disproved. In fact, it's necessary to replace water lost through sweating to prevent heat exhaustion. This is best done by occasional drinks of small amounts of water, perhaps half a glass.

Salt needs to be replaced daily, particularly during the acclimatization period. Extra salting of food within the bounds of taste will accomplish this. Salt tablets, particularly on an empty stomach, can be irritating and may be poorly absorbed. Adding one teaspoon of salt to six quarts of water used for drinking during hot-weather workouts offers another approach.

Frequent rest periods during hot weather workouts are recommended. Coaches are urged to watch players closely for signs of lethargy, inattention, stupor, awkwardness or unusual fatigue. Symptoms of water and salt depletion may include headache, nausea, hallucinations and weak and rapid pulse.

The AMA Committee, composed of physicians with particular interest in sports medicine, offers some points to help coaches prevent heat exhaustion and heat stroke in their young players:

1. Require a careful medical history and check-up prior to beginning of practice.
2. Schedule workouts during cooler morning and early evening hours in hot weather.
3. Acclimatize athletes to hot weather by carefully graduated practice schedules.
4. Provide rest periods of 15 to 30 minutes during workouts of an hour or more in hot weather.
5. Supply white clothing (to reflect heat) which is loose and comfortable (to permit heat escape) and permeable to moisture (to allow heat loss via sweat).
6. Furnish extra salt and water in recommended amounts.

Symposium On Cutaneous Toxicity Set In Washington, D. C.

Questions related to testing topical agents, such as drugs, cosmetics, industrial and household products for toxicity will receive a timely and thorough airing at a Symposium on Cutaneous Toxicity to be held October 26-27 in Washington, D.C., (Mayflower Hotel).

Co-sponsors are the Society of Toxicology and the American Medical Association Committee on Cutaneous Health and Cosmetics.

Subjects covered by the symposium's 15 speakers will range from previously classified or unpublished areas of investigational knowledge to current views of the Food and Drug Administration in regard to safety testing. All the subjects bear upon proposals for pending FDA legislation and regulations to require that manufacturers prove their products safe for human use.

The speakers, representing university laboratories, industry, and relevant government agencies, will appear at four sessions.

The topics: Session I—Absorption, Nature of the Threshold Barrier, Percutaneous Toxicity, and Sensitization Mechanisms; Session II – Pharmacogenetics, Predictive Testing Procedures-Irritation and Sensitization, Biometrics, and Clinical Aspects of Irritation and Sensitization; Session III—Need of Methods, Methods of Evaluating Skin Irritation, New Data on Eye and Skin Tests, and Skin Carcinogens; Session IV—Species Aspects and Human Correlation, Man vs. Animal Eye Testing, and Current Viewpoint of the FDA. The final session will end with a roundtable discussion and a question-answer period.

Moderating the four sessions will be: Harry W. Hays, Ph.D., Advisory Center on Toxicology, National Academy of Sciences, National Research Council, Washington, D.C., president of the Society of Toxicology, and a member of the AMA committee; Adolph Rostenberg Jr., M.D., professor of dermatology and head of the department, University of Illinois, Chicago, and member of the AMA committee; Raymond R. Suskind, M.D., professor and head, Division of Environmental Medicine, University of Oregon, Portland, and chairman of the AMA committee; and Fred Coulston, Ph.D., president-elect of the Society of Toxicology, editor of the Journal of Toxicology and Applied Pharmacology, and professor of experimental pathology and toxicology, and director of the Institute of Experimental Pathology and Toxicology, Albany Medical College of Union University, Albany, N.Y.

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HIPPOCRATES: MEDICINE BECOMES SCIENCE (see page 717)

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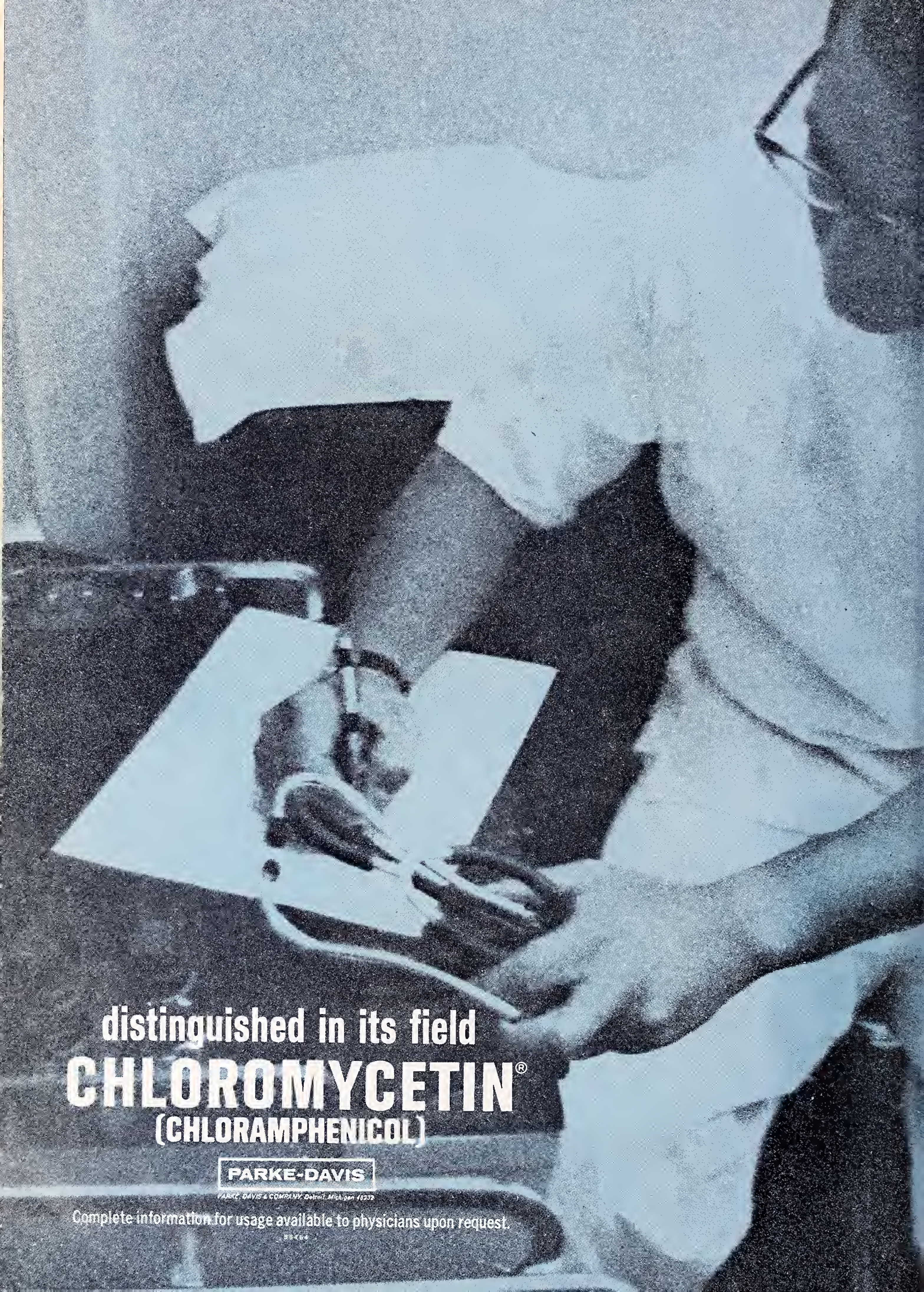

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editorials

Science Tools:
8. The Apex Cardiogram (ACG)

In 1956 Dr. E. G. Diamond visited the laboratories of Dr. Hartman in Holland and came back with an interest in the apex cardiogram (ACG) which he has actively pursued ever since. The ACG is a record of chest wall vibrations not audible to the ear but electronically recorded. These vibrations are set in motion by cardiac contraction and are recorded on an instrument called the apex cardiogram ACG. It is an attempt to get as close as possible on the intact human to the sources of cardiac activity. A little cup is placed on the apex while the patient is on his left side. The curves recorded represent actual displacement of the chest wall and a precordial movement caused by expansion and contraction of the ventricle. There are several waves in the record. One is termed the "a" wave and precedes the main one which represents the pushing of the ventricle during systole. The "a" wave represents the extra distension of the ventricle during atrial contraction.

The "a" wave amplitude in relation to the total amplitude of the tracing is what Diamond and his associates have studied in a variety of normal and abnormal states especially ischemic heart disease (IHD), during exercise and during smoking. In normal subjects the "a" wave is very small or even absent. With exercise or smoking this "a" wave increases sometimes from nothing to an amplitude of about 20-40 per cent in relation to the total amplitude of the tracing. Simultaneous recordings of intra-ventricular pressures and the apex cardiogram revealed that the "a" wave is caused by atrial systole causing increased ventricular filling and raising the end-diastolic pressure.

The abnormalities of the ACG in patients with IHD and effect of exercise and glyceryl trinitrate were reported in previous papers.[2,3,4] In a recent report[1] they found that venous tourniquets and tightly applied abdominal binders usually reduced or actually prevented in some cases the post-exercise increase in the "a" wave of these patients. The study consisted of observing 10 normal subjects and 40 with IHD. In normals the "a" is very small whereas in patients with IHD it is very large. Simultaneous determinations of intracardiac pressure and the ACG were obtained during and after application of tourniquets and abdominal binders in 5 patients. At the time cardiac output was also determined by an indicator dilution technique. The "a" wave declined in subjects with IHD after application of a tourniquet or an abdominal binder or after glyceryl trinitrate. On release of tourniquet or belt the "a" wave promptly returned to the original level. Similarly there was a post-exercise increase in the amplitude of "a" which was minimized or completely prevented by application of the belt or tourniquet prior to exercise with a rebounding increase in the amplitude of the "a" after relaxing. The similarity of effects on the end-diastolic left ventricular pressure and on the ACG by glyceryl trinitrate, abdominal belt, and

THE COVER

HIPPOCRATES: MEDICINE BECOMES SCIENCE

THE ART of medicine in the ancient world developed to its highest point in Greece, during the millennium between 500 B.C. and 500 A.D. This creative period is symbolized by Hippocrates, the "Father of Medicine," whose name has come to represent the beauty, value, and dignity of medicine for all times. Hippocrates' kindliness and concern are embodied in his aphorism, "Where there is love for mankind, there is love for the art of healing." These qualities are reflected in the face of this revered practitioner, scientist, and teacher, as he palpates a young patient and attempts to soothe a worried mother sometime late in the fifth century B.C.

tourniquets suggests that at least one of the therapeutic actions of nitroglycerin in angina is related to venous pooling.

The value of the ACG is bound to increase as more studies are made correlating this graph with other hemodynamic events which at present require catheterization, cut down, dye, angiograms and other difficult and time consuming procedures. Already it has offered an explanation for an observation made by Kerr Cannon and Lagen[5] in 1934 that patients with coronary disease and with thick abdominal walls were improved both in the frequency and severity of attacks of angina pectoris by the application of an abdominal binder. They speculated that the improvement was the result of an improved cardiac output. The actual explanation from ACG studies, however, is that there is a decrease in venous return to the right side of the heart by a binder and no increase in cardiac output. The mechanism by which tourniquets and binders minimize the abnormal changes in the "a" wave of the ACG appears to be related to a decrease in the left ventricular end-diastolic pressure which in turn may be a result of decrease in the blood volume.

We have long known from clinical observations that venous tourniquets improve cardiac function in congestive heart failure especially in patients with acute pulmonary edema. The mechanism by which the venous tourniquets improve cardiac function in these circumstances seems to be related to a decrease in the filling pressure with consequent "unloading" of the heart. Even in normal patients venesection and applied tourniquets cause a fall in atrial pressure from 20-65 mm. H_2O without significant changes in cardiac output.[6] Similarly Howarth's studies[7] on venesection and pressure cuffs revealed their effectiveness in reducing right atrial pressure which is associated with an increase in cardiac output in patients with heart failure due either to hypertension or IHD. The ACG appears therefore to be a useful tool to detect and therefore objectively document such physiological changes.

It has already given rise to further questions. Why is the end-diastolic pressure elevated in angina pectoris in the absence of "left ventricular failure." Can it be that the ischemic ventricle is rigid? Does ischemia produce a loss of compliance? To be sure the prominent "a" of the ACG is but a crude and indirect measurement which may with refinement prove useful in diagnosis and therapy. One such new approach will come from an analysis not only of the "a" wave but the whole diastolic movement of the apex cardiogram which is related to ventricular filling. The speed of filling of the ventricle appears to be directly proportional to the slope of the filling wave of the ACG. This would appear to be a simple, easily reproducible measurement which can be made in the patient with mitral valve disease. If this turns out to be valid it can replace catheterization and angiography for deciding if the mitral lesion is primarily regurgitation or stenosis.

L.H.N.

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Carbon Dioxide Inhalation In Cerebral Vascular Disease

There is ample evidence that the cerebral vascular system possesses a marked degree of autonomy which is largely unaffected by changes in the systemic circulation. This autonomy is made possible because the brain circulation is not materially affected by either the sympathetic or parasympathetic nerves to the brain vessels even though the autonomic system plays a major role in regulating the peripheral circulation. This leaves the brain free to regulate its own blood flow, a process termed autoregulation. The brain does this because its vessels are powerfully responsive to carbon dioxide concentration and to a lesser extent oxygen concentration. If a subject is allowed to breathe air with six per cent carbon dioxide concentration the cerebral blood flow increases approximately 100 per cent. A decrease of arterial oxygen saturation to 75 per cent increases the blood flow approximately 40 per cent. This shows that oxygen lack in the physiological range is about one half as potent as carbon dioxide excess in increasing cerebral blood flow.[1,2,3]

Carbon dioxide concentrations of 5-7 per cent in inspired air produces also peripheral vasoconstric-

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tion and some rise in arterial pressure. As a result of this combined action (cerebral vasodilatation and increase of perfusion pressure), a greater blood flow will take place in the brain but no increase in cerebral oxygen consumption which remains remarkably constant during intellectual and muscular activity and during sleep.[4]

The response of the cerebral circulation to carbon dioxide in pathological states has been studied in great detail. Most of the evidence suggests that inhalation of five per cent CO_2 can dilate the cerebral vessels and can increase cerebral blood flow even in the presence of vascular disease. Some, however, have found no response in normotensive patients with arteriosclerotic disease of the brain[5] while others report a clear response to five per cent CO_2 both in normotensive and hypertensive patients with cerebral arteriosclerosis even those patients with focal cerebrovascular disease.[6] The preponderance of opinion, however, is expressed by Sokoloff[7,8] who states "Even though there may be sufficient disease in the cerebral vessels to raise cerebrovascular resistance and reduce blood flow markedly, there still remains a considerable degree of labile tone which can be reduced by CO_2."

Fieschi, Alessandro and Galbo[5] have investigated this problem. They studied the cerebral hemodynamic response to the inhalation of five per cent CO_2 in aged patients without vascular disease and in patients with cerebral vascular lesions. There were of course significant individual differences. They found no difference between the control group and the cerebral vascular disease group in pulse rate, blood pressure and respiration, all of which increased somewhat. Patients with diffuse angiosclerosis, deficient parietal filling, substenosis of common carotid artery, subocclusion of the middle cerebral artery, dilatation and deficient parietal filling of the internal carotid artery, were carefully studied. On the whole the increase in cerebral flow after one minute was less than normal. After two minutes the increase in cerebral blood flow rose to 47 per cent, still less than normal, but after six to seven minutes of inhalation the percentage increase rose to 98 per cent. In short inhalation of CO_2 at five per cent concentration increased the caliber of cerebral vessels and cerebral blood flow in patients with cerebral vascular disease as in normals, but a great variability was observed from case to case.

From a practical standpoint it is possible to draw certain conclusions from this work. The response of cerebral circulation to inhaled CO_2 varied of course in cerebral vascular disease but was normal in over half of the subjects. In one-third the response to CO_2 was abnormal not in absolute diminution but in the slower rate of response. In view of the lack of metabolic reserves of the brain and its extreme sensitivity to hypoxia, it is most important that the cerebral circulation should be able to adapt promptly to circulatory changes. Since many patients with cerebral vascular disease can increase their blood flow by means of CO_2 inhalation we are in possession of a powerful tool to assist such patients in their cerebral function. How often such procedures should be tried and what the outcome of such treatments will be in terms of permanent improvement of cerebral function is the next step in the evaluation of this potent method of increasing cerebral blood flow.

The clinician is constantly searching for adequate methods of increasing blood flow to organs poorly irrigated because of degenerative vascular disease. As far as the brain is concerned, we have known for a long time that cerebral dilatation is not affected by presently available drugs. Producing hypercapnia, however by CO_2 inhalations is a potent vasodilator in health as well as disease and deserves a more important place in the treatment of cerebral vascular disease than it has thus far occupied.[9]

CO_2 inhalation is frequently used to hasten recovery from general anesthesia since it stimulates respiratory elimination of volatile anesthetics and clears this agent from the tissues of the central nervous system more rapidly as a result of the accelerated blood flow through the brain. The addition of five per cent CO_2 to inspired air should be effective in counteracting the deleterious effects of low oxygen in intellectual functions. When oxygen supply to the brain is low, CO_2 inhalation can be beneficial first by stimulating pulmonary ventilation causing greater oxygen uptake by the arterial blood. Second by producing moderate increase in blood pressure by peripheral vasoconstriction so that more blood can flow through the brain whose vessels are dilated by the CO_2.

There are also times during circulatory collapse or secondary shock when CO_2 inhalation may be beneficial by dilating cerebral vessels constricting peripheral vessels and leaving the coronary vessels unchanged. Here CO_2 redistributes the cardiac output to favor the brain at the expense of less vital tissues. It may even combat the arterial hypocapnia resulting from the hyperventilation not infrequently seen in secondary shock. For when this occurs, it will tend to reduce CO_2 concentration and jeopardize the circulation through the brain. Sometimes a dose of morphine, by depressing respiration, restores the arterial carbon dioxide concentration which in turn restores the cerebral

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blood flow towards normal thereby causing a dramatic improvement in the mental state.

It is clear that understanding the physiology of carbon dioxide furnishes explanations of many procedures which can be of benefit in treatment of patients with cerebral vascular insufficiency.

L.H.N.

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Suppression Of Glandular Activity: 1. Feedback Mechanisms

Suppression of glandular activity is an established principle in clinical therapeutics. Some glands can be suppressed directly as, for example, the thyroid by thiouracil. Some can be controlled utilizing the feedback mechanisms involved in endocrine regulation. Although this mechanism operates somewhat differently with different glands, its meaning may best be explained by the description of an actual situation which has very real and practical implications. Take for example endocrine organ A (anterior pituitary) when stimulated by "certain factors" releases hormone A (ACTH). Its increasing titre in the blood now stimulates endocrine organ B (adrenal cortex) to produce and release hormone B (cortisol). As ACTH continues to stimulate the adrenal cortex, the increasing blood concentration of cortisol begins to exert an inhibiting effect on organ A (anterior pituitary). As a result, the latter reduces its output and eventually ceases to release ACTH. Thus cortisol serves not only its particular function in the body, but it also regulates its own production by its inhibitory effect on the anterior pituitary.

Here we must remember that as long as the question is only one of equilibrium between the two organs of internal secretion, we do not introduce the function of the nervous system in this equation. However, endocrine organs cannot by themselves make decisions on the basis of the feedback information of the type described above. For example, conditions may change in such a way that the anterior pituitary can continue to stimulate its target organ irrespective of the blood titre of the adrenal or gonad or thyroid. Such cases are well recognized in clinical medicine and will be dealt with subsequently. Conversely, the anterior pituitary can stop releasing its hormone even though the target gland has hardly begun to respond to the stimulus from the anterior pituitary. In order to respond to such adjustment, the feedback cycle must be open in order to allow the messages that may change the existing pattern. Ovarian function serves to illustrate this point.

The mechanism for release of gonadotrophins in mammals was originally conceived as a simple feedback of gonadal steroids to the pituitary.[1] Scharrer[2] however points out that if this were the only determining factor, then external and internal conditions such as photoperiods, availability of food, social contacts, etc., could not affect the reproductive cycle, whereas, we know they do. It is clear that channels must exist through which these modifying influences enter into the control system even to the point of superseding the ovarian feedback mechanism. This integration of course can only take place in the central nervous system. Scharrer reminds us that this principle applies not only to mammals but to other animals as well, including insects.

In the same way, what has been said above to the effect that the secretion of hypophyseal adrenocortical hormone ACTH is regulated by the blood levels of cortisol, is no longer considered adequate to explain adrenal cortical function. Here too, control is exerted by the central nervous system and the hypothalamus.[3] A recent report of periodic disease referable to overactivity of the hypothalamus and resulting hyperadrenocorticism is a case in point.

There is no doubt that the presently available data are adequate to support the concept of hormonal pathways terminating in the central nervous system and of nerve cells capable of responding to hormones. There is a very close link between the nervous system and organs of internal secretion namely, the neurohormones. These can act directly on affected organs. They can promote water absorption by the kidney. They can stimulate smooth muscle in vertebrates. They inhibit gonadal maturation in Annelides and Crustaceans. But in many instances, the neurohormones activate other endocrine glands, as for instance, the adenohypophysis of vertebrates releases ACTH by action of vasopressin and prolactin by action of oxytocin.

The majority of endocrine glands are not under direct nervous control. The neurosecretory cells however constitute the link between the central nervous system and the organ of internal secretion. As both nerve and secretory cells they are enabled to receive and to "understand" nervous impulses from other neurones and to "speak" to the organs of internal secretion in their "language" by dispatching chemical messages. Scharrer states it this way, "the proposition that neuroendocrine systems of basically similar design in invertebrates and vertebrates control vital processes on cues received and integrated by the nervous system, and that groups of neurosecretory cells function as translators between nervous and endocrine systems is now well documented and its general applicability accepted."[2]

Even though the endocrine regulation is more complicated than the idea of a simple feedback mechanism, the fact is, it is possible to suppress glandular activity by administering its hormone and thereby inhibiting the formation of its adenohypophysial stimulating hormone.

L.H.N.

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Reflections On Obesity

Overweight constitutes not only a life-shortening situation but a social problem of great importance. One would therefore suppose that the obese patient seeking the physician's help to reduce weight, would be well motivated and persistent in his effort to achieve the aim of normal weight. However, conventional treatment generally fails or shows only temporary results.

Most physicians believe that extensive intake of calories is the most important cause of obesity, and when a balance does not exist between intake and output of energy there must result either a gain or loss of body weight. Their attitude therefore is that the intake must be curbed enough to restore balance and or metabolism must be increased to increase the output. Accordingly when a reduced diet does not result in a weight loss in the patient, the physician reasons that knowingly or unknowingly the patient is miscalculating his intake.[1]

One reason for the conventional failure of treatment of obesity is that we do not know for sure whether a certain caloric intake will produce a safe weight loss in a particular person living and working in a particular environment. We do not know the individual's basal caloric requirements and how many calories the patient uses up in living and working. A simple equation to keep in mind is: intake of food energy = output of energy (physical activity and metabolic expenditure) ± stored energy as body tissue principally fat.

The amount of food consumed is the result of complex factors of appetite hunger, satiety, as well as psychological ones notably anxiety and depression. It is clear that control of this first half of the equation, that is food intake must continue to be a major force in treatment. What about the second half of the equation. Specifically can a reduction in physical activity lead to obesity. The above equation says *yes* and this has been shown experimentally on rats with enforced inactivity.[2] And of course it is also well known that obesity of hyperphagia can be limited by high levels of enforced exercise.

Many obese persons are known to be less active than non-obese. As people grow older all men and women become more quiescent and begin to accumulate obvious fat. In fact the onset of corpulence often begins with a decline in activity not accompanied by a reduction of caloric intake. In the obese teenager a low level of activity is a known cause of obesity as is consuming more calories.[1] Clearly the physician should not ignore the importance of lowered body activity and it would seem profitable whenever possible to introduce extra-activity in any regime designed to prevent weight gain or reduce obesity.

It is wrong to assume that exercise will increase appetite and therefore will not lead to weight loss. It very well might. Another false assumption is that basal energy requirements remain the same. The fact is that basal energy requirements decline progressively from a very young age to the oldest age. This presents a problem quite distressing for some people, because it means that if an adult does not increase his physical activity as he grows older, an event unlikely and often unwise, then he must every year decrease, certainly never increase his food intake if he is to avoid gaining weight. This

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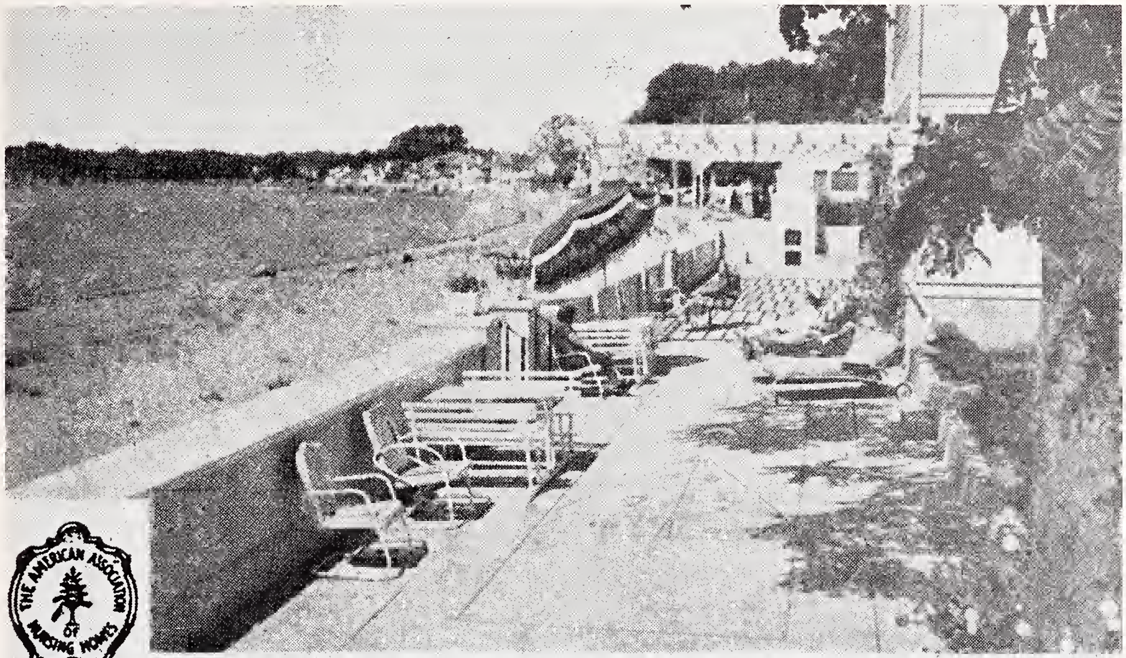

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problem is especially frustrating to the obese patient who must continually and permanently restrain his appetite. This might contribute to the high percentage of people who regain weight after an initial loss.

The slow rate at which weight can be lost safely on a calorically deficient diet is very irritating to many patients who must see results in a hurry. When they discover that with a minimal restriction of intake, they soon reach a weight at which no further weight loss occurs, they seem frustrated. To lose more weight the patient must again cut his intake of food or increase his physical activity even more until the restricted caloric intake just equals the need, because the loss of tissue reduces the metabolic cost of living.

Besides physical activity in the second half of the equation there is the problem of metabolic expenditure. The older physiologists believed that there is no difference between the obese and non-obese person metabolically and the obese differs from the non-obese only in the ingestion of excessive amounts of energy. There was then no information on metabolic efficiency or on the relative amounts of adipose tissue in the organism. We all recognize different efficiencies among people in the performance of physical activity. People differ in how efficiently they accomplish the same maneuvers and one individual might extract more usable energy from a given amount of food. If there developed a minimal gain in the efficiency of some cellular processes, over a period of time less calories would be used for the same work and obesity would slowly develop. This has been definitely demonstrated in mice by Swift and Black[3] who found mice on a high fat diet to outgain those on the same amount of high carbohydrate calories. More recently Fenton and Marsh found a strain of mice that develop obesity when they are fed high fat diets.[4] This strain shows a hereditary predisposition towards a more efficient use of fat. Their metabolic cost of metabolizing and storing fat is less than when dealing with a large carbohydrate load and thus more calories are available for storage. Can it be that similar differences exist in man?

Hereditary and metabolic obesity clearly exists on many strains of farm animals that have been selectively bread to produce fat but it has been most extensively studied on mice by means that damage nuclei in the hypothalamus.[5,6,7] Another type was discovered by Ingalls, Dickie and Snell in 1950.[8] This strain shows a greater degree of obesity, a high blood glucose, is remarkably resistant to insulin, cannot raise its heat production during a cold stress and on a weight basis has a much lower metabolic rate than the animals with hypothalamic induced obesity. This means among other things that lipogenesis is proceeding at the expense of other tissues even when calories are restricted. If the laws of thermodynamics do hold for all animals, non-obese and obese alike, then what an individual organism does with its energy intake will vary according to its own particular metabolism. If mice exist which have an obligatory production of fat of hereditary origin why cannot this phenomenon also exist in man. The fact is that it probably does.

We know now that adipose tissue is an active and major site of fatty acid synthesis. Lipogenesis proceeds at a very slow pace in the fasted normal animal and ceases altogether in the diabetic. In the absence of insulin enzymes for fatty acid synthesis are inoperative. In the presence of insulin prolonged intake of excess calories is accompanied by a tremendous increase in the ability of fat cells to take up carbohydrate and synthesize fat. This prolonged overfeeding always changes the preferred pathway for the handling of glucose to one favoring the synthesis of fat. Since insulin is basic in this whole process, excess food intake requires more insulin and leads to more ready exhaustion of the pancreas. This is probably the reason for the high incidence of diabetes in the obese person.

If the metabolic pathways shift to lipogenesis might this not explain the difficulty experienced by some obese patients in attempting to lose adipose tissue permanently. Whether the metabolic difference between the normal and obese patient is due to obesity itself or causes obesity, the fact is treatment will require a shift in the enzymatic machinery of the cell away from lipogenesis and in the direction of the mobilization of fat. Epinephrin injections stimulate the sympathetic nerves to adipose tissue and increase rate of lipolysis and release of fatty acids. So does starvation. Epinephrin is not clinically feasible but starvation periods are. Gordon has shown that patients with "resistant obesity" i.e., those who lose weight with difficulty when their caloric intake is decreased, will reorient their enzymatic machinery away from lipogenesis to lipolysis after periods of starvation.[9]

It is likely that the mobilization of fat is affected by many normally occurring substances. Debons and Schwartz[10] have shown that thyroid hormone is necessary to the action of epinephrin in the release of fatty acids. This probably explains why little or no release could be obtained from the tissues of the hypothyroid animal. There may be other substances such as Chalmers, Kekwick and Powan[11] found in human urine.

The failure to lose weight on a prescribed diet creates a situation that is disappointing to the patient and discomforting to the physician. The physician usually contends that the diet is not being followed and most of the time this is true. However, we must recognize that there are some obese individuals who do not show a loss of weight on an extremely low caloric intake, as low as 600 calories. In some the apparent lack of weight loss is due to the retention of water. The question remains why these individuals retain water.

Out of these studies have come several revealing conclusions. The need to restrict calories, the need to increase activity, the need to shift the enzymatic machinery away from lipogenesis, by short periods of starvation and by the use of thyroid derivatives that aid in fat mobilization. Clearly the question of differing metabolic efficiencies is an imposing challenge to workers in all disciplines related to human nutrition.

L.H.N.

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The Role Of Coronary Artery Spasm In Myocardial Infarction

Vascular reactivity seems to play a significant role in blood flow through organs over and apart from general factors regulating arterial pressure. In the coronary arteries Andrew[1] has shown rapid and to some extent rhythmic oscillations or constrictions of the vascular walls which appear to be independent of general factors. As the oscillations increase so does the blood flow, and vice-versa. Inadequate vascular reactivity frequently occurs in pathologic situations, in some acute infections like dysentery and pneumonia and also in acute myocardial infarction. In these and other instances the vaso-motor activity is strikingly decreased and close to exhaustion causing a greatly reduced coronary blood flow.

It is not difficult to see how a reduced coronary flow would impair the regenerative processes especially after infarction has caused necrosis of some tissue. If vascular reactivity is an important factor in blood flow, it is essential that we learn the physiology of reactivity. Perhaps it could lead to improvement of the reparative processes following myocardial infarction, and therefore become of great potential usefulness.

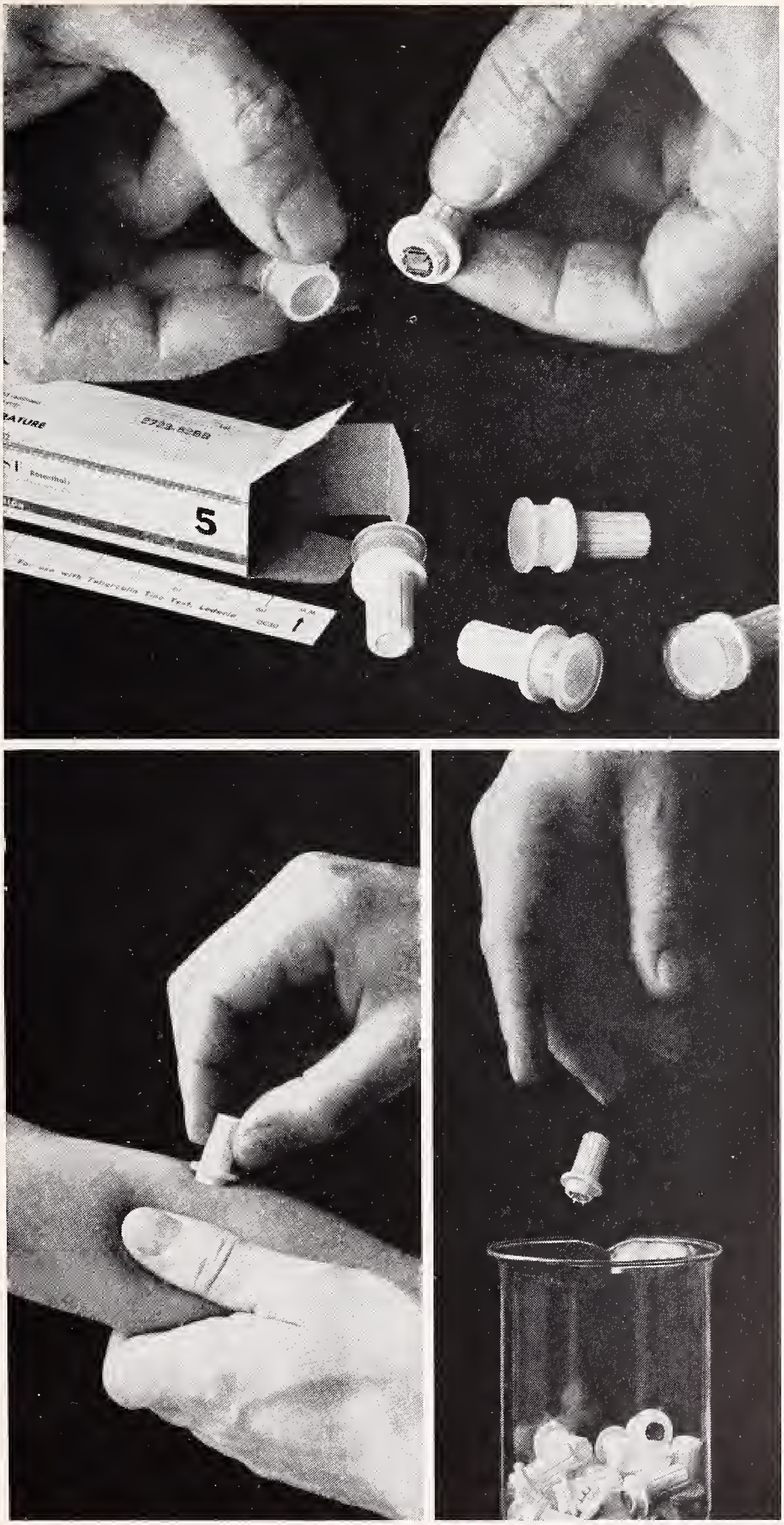
The beautiful techniques employed to record coronary blood flow, and coronary vessel reactivity are briefly described by the Soviet investigator in a recent publication of Circulation.[1] Hundreds of experiments are reported on rats, rabbits, dogs and humans of all ages that died of various causes without and with coronary artery disease.

In the blood supply of heart muscle arterial oscillations seem to have a definite significance since with greater amplitude of the oscillations there is twice as much blood flowing through the myocardium as in the type in which there is found little or no oscillation. With this method numerous observations on the condition of the blood flow during acute infarction, angina pectoris and coronary insufficiency and following the administration of drugs became possible.

In angina pectoris and coronary insufficiency there is an increase in oscillation which tends to enhance the blood supply, a useful adaptive mechanism. Since we know from other work, that reactive hyperemia is set up by the liberation of bradykinin it might be that this polypeptide is more readily liberated in exercise, angina pectoris and hypertensive disease states in which the heart needs more blood.

Epinephrine seems to decrease oscillations of cardiac vessels and proportionately reduce coronary flow. This is an important finding and explains why epinephrine when liberated during emotion is bad for patients suffering from angina pectoris.

In the acute stage of myocardial infarction, the majority of animals, seven out of eight, showed widespread constriction. The same spasmodic reactions in the coronaries were demonstrated after traumatic shock and cranio-cerebral injuries. In an attempt to overcome the constrictive effects, the author found nitroglycerin ineffective as was digitalis. However, aminophyllin was found to have some slight coronary dilator influence. In general,



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vasoconstriction was widespread in the coronary arteries of dogs after myocardial infarction.

These findings have raised an important question for which an answer is urgently needed. What part of the necrotic process in ordinary myocardial infarction is due to the obstructed artery and what portion is caused by the associated vasoconstriction? This is a very difficult question to unravel but one which could be solved if early in the disease the clot obstructing the coronary artery could be dissolved. The reestablishment of the circulation would be expected to wash away the vaso-constrictor substances and thus eliminate the factor of vascular spasm. We are on the threshold of just such a breakthrough in fibrinolytic therapy. Both enzymatic and non-enzymatic fibrinolytic agents are under intensive examination, and it should not be too long before a definite answer will be at hand as to the role played by coronary spasm in the size of an infarct and therefore in the outcome of myocardial infarction.

L.H.N.

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A Simple Method To Measure Estrogenic Activity: The Vaginal Cytogram

The idea that the menopause is a "natural" state and therefore should be allowed to continue without medical interference is one of those medical dogmas that have been difficult to dislodge. Many rationalizations have been indulged in to justify this dogma. One was that exogenous estrogens may be carcinogenic. This has been definitely ruled out by the studies reported by Bishop.[1] Another argument was that in some patients, the recognized symptoms of the menopause such as hot flashes, nervousness, sweating, may not respond to estrogen therapy, and therefore estrogenic substances are really ineffective. A third argument was that estrogenic therapy may cause breakthrough bleeding which in a senile uterus with a stenosed cervix might cause serious discomfort. A fourth objection for the use of estrogenic supplement therapy was the intolerance which some women exhibited to the use of diethylstilbestrol.[1] Such arguments however, only tell a part of the truth about estrogenic supplement therapy.

There is another aspect of the problem that has received less attention than it deserves. Since 1952 it has been known that it is possible to inhibit the development of coronary atherosclerosis by estrogens in cholesterol fed chicks.[2] There is good evidence gained also from observations in humans that there is a rising incidence of coronary artery disease after the occurrence of a state of estrogenic deficiency.[3] Furthermore, there has been demonstrated that estrogens exert a beneficial effect on female patients with senile mental conditions.[4] Finally, Lin and Lin[5] have recently reported that some of their patients not only lost the symptoms of hot flashes, nervousness and sweating but gained in other respects such as increased sex drive and enjoyment of sex activity.

The real difficulty in the proper management of the menopause has arisen from failure to establish the actual degree of estrogenic deficiency in any single patient. This was not due to any lack of method to determine the state of estrogenic activity in any individual patient, but rather the failure to utilize the vaginal cytogram to establish the degree of estrogen activity. Women vary considerably in the amount of estrogen secreted by their ovaries or adrenals after the menopause. Lin and Lin found as many as nine out of twenty-four patients with a natural menopause, who showed satisfactory estrogenic activity. The remainder varied considerably, the castrated female showed absence in estrogenic activity within two to seven days while the patients with a natural menopause may or may not show estrogen deficiency for two years.

It is clear that the marked variability of estrogenic activity found in patients after the menopause is due to varying states of deficiency in each patient and that a satisfactory method of determining this would clarify the whole problem of estrogenic supplement therapy. The best, simplest, cheapest, and most reliable method for establishing the existence of estrogenic activity is the vaginal cytogram. This has been known since 1933 when Papanicolau[6] showed that the degree of cornification of the vaginal epithelium is a reliable method of determining the amount of estrogen in the blood. It is more reliable than the assay of estrogen degradation products in the urine which does not correlate too well with the level of estrogen in the blood and is moreover a complicated method beyond the reach of the practicing physician.[7]

A vaginal cytogram properly prepared is comparable to a differential count of white blood cells. If there is a specific vaginal infection as in trichomonal vaginitis, it is readily recognized. In a cytogram which does not show infection, then an elevated cornification count indicates a good estrogenic effect. If one obtains reliable daily or biweekly serial vaginal smears from young healthy women having regular menstrual periods, then the percentage of cornified cells clearly indicates each phase of the menstrual cycle. In the follicular phase, the cornified count is 20 to 50 per cent. In the preovulatory or ovulatory phase, the count rises to 60 to 85 per cent. In the luteal phase it drops to 20 to 40 per cent once more. In short the vaginal cytogram offers a reliable measure of estrogenic activity, much as the basal metabolic rate does of thyroid activity.

In the absence of vaginal infection, a properly performed vaginal smear is a simple, rapid, inexpensive and reasonably reliable method of evaluating the hormonal status of a gynecological patient. It can be used for the titration of ovarian hormonal activity in the human. It is accepted as an important procedure in the evaluation of the hormonal status of surgically castrated women as well as those undergoing the menopause. Apparently it has not been used as a guide to the treatment of patients as widely as its value merits.

Lin and Lin[5] studies of surgical castrates and normal menopausal women, showed clearly that the improvement of symptoms was generally related to the improvement in the cornification count. A cornification count of 30 to 40 per cent obtained by replacement therapy, indicated a satisfactory level for ameliorating symptoms without producing estrogenic side effects such as nausea, vomiting, soreness of the breasts. If the cornification count rose above 40 per cent, break through bleeding might occur and thus the vaginal cytogram was found to be an excellent method of titrating dosage of estrogenic replacement. The authors found several patients that showed intolerance to the oral synthetic preparation, diethylstilbestrol, but without such side effects when given estrogenic substances conjugated (Premarin). Women who discontinued their estrogenic therapy showed a recurrence of symptoms and a sharp reduction of the percentage of cornified cells in the vaginal cytogram. When these same women resumed their estrogenic supplement, the symptoms disappeared and the vaginal cytogram again mirrored the effect of endogenous and exogenous estrogen.

The same authors found that the interval between the menopause and the appearance of symptoms is much shorter in the surgical castrated patients. On the other hand, in the postmenopause, the decrease of estrogen production was rather slow. Some patients showed persistently good estrogenic effects, evidence in support of Hertig's[8] contention that the stromal cells of the ovary might assume secretory function.

The most satisfactory amount of exogenous estrogen to be administered is that amount which will produce 30 to 40 per cent superficial cells. Since the natural postmenopausal woman needs definitely smaller doses of exogenous estrogen than the surgical castrate, it indicates not only that the aging ovary can produce some endogenous estrogen, but also that with the vaginal cytogram as a guide, it is possible to administer an amount of exogenous estrogen safely and physiologically to the natural postmenopausal woman, without producing untoward breakthrough bleeding, resulting from a hyperplastic endometrium. It is also obvious that when the vaginal cytogram shows satisfactory estrogenic activity, while the patient's symptoms of flashes and nervousness persist, then the symptoms must be considered completely unrelated to estrogen deficiency. It is needless here to point out that if unexplained genital bleeding occurs after the menopause, the patient must be examined by curettage to rule out malignancy.

Lin and Lin make a plea that in both the natural postmenopausal and the surgically castrated patient, estrogenic therapy be employed regardless of symptoms, or their absence, if there is any objective evidence of estrogenic deficiency in the vaginal cytogram. Not only will such patients feel better, but coronary atherosclerosis might be allayed or prevented, and certain senile mental conditions will be improved.

L.H.N.

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Lycanthropy And Porphyria

Science is the professed enemy of superstition and unreason, and medicine has often offered explanations in terms of pathology for phenomena previously attributed to supernatural causes. In

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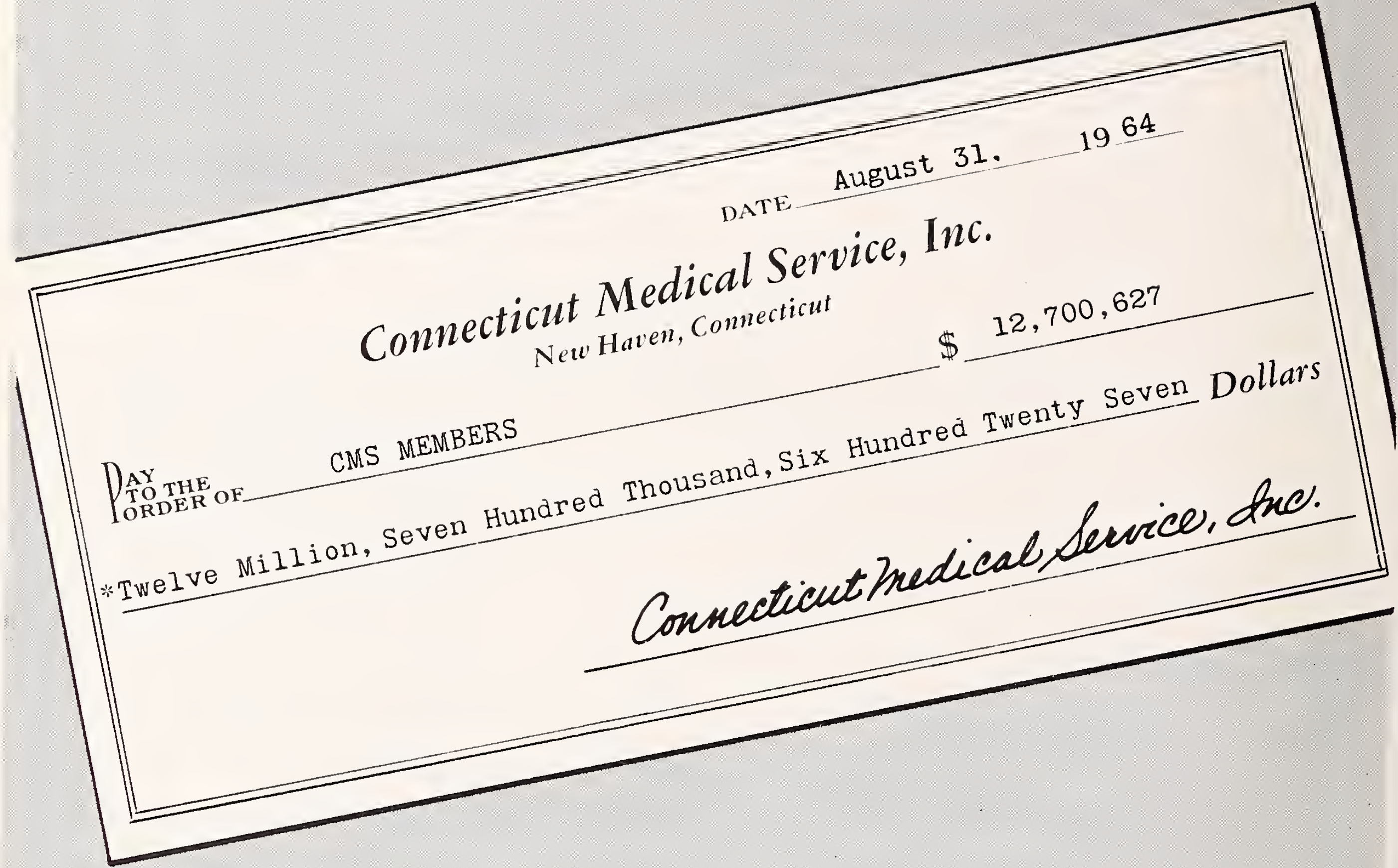

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a curious essay, Illis[1] attempts to explain the werewolf in terms of a disease process, and offers intriguing analogies between the descriptions of these creatures and of patients with porphyria.

Werewolves, or men transformed into wolves, were described by such Greek and Latin writers as Pliny, Herodotus, and Virgil. Belief in such transformations reached its height in the Middle Ages, and survives today in certain isolated areas of Europe. Women and children were sometimes affected, and several references to a number of werewolves in the same family are cited. Until the beginning of the seventeenth century, werewolves were regarded as heretics in Europe, and were subjected to the treatment usually given to heretics.

The usual description of a werewolf refers to his pale yellowish or greenish skin, with multiple excoriations, and his red mouth. The eyes are sunken and unsteady. The creature tends to roam at night and to exhibit disordered behavior.

Illis reasons that such a widespread belief in both time and place must have some factual basis, and suggests that the clinical features of porphyria could be combined in individuals so as to simulate the legendary picture of the werewolf. The congenital and cutanea tarda varieties of this disease are both characterized by varying degrees of photosensitivity, with the production of vesicular erythema. These skin lesions may ulcerate and eventually underlying cartilage and bone may be attacked. Hypertrichosis and pigmentation may develop. The hepatic types are often accompanied by jaundice. Reddish discoloration of the teeth may be present because of deposition of porphyrins. The acute intermittent type is prone to involve the nervous system, but this may occur in the other varieties as well. Mental disorders of all types and convulsions have been described. The victim may choose to wander about at night because of photosensitivity and disfiguration.

These features, when combined, seem to fit well with the ancient and medieval descriptions of the werewolf. The presence of such an individual in a primitive and superstitious community could certainly call forth a supernatural explanation.

H.L.

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Serum Iron

Many clinical laboratories are now doing determinations of serum iron (SI) and total iron binding capacity (TIBC). The techniques require scrupulously clean glassware; other than this there are no unusual technical difficulties in performing the analysis. Knowledge of these serum factors can be very helpful and it is the purpose of this discussion to indicate the normal values and the meaning of variations. We are grateful to Dr. S. Raymond Gambino of the Englewood Hospital, Englewood, N.J., for permission to quote the following material from the February 1964 Critique he prepared for the Council on Clinical Chemistry of the American Society of Clinical Pathologists.

Normal Values

The normal range for SI is commonly given as 60 to 180 ug./100 ml.[1] However, the SI level varies throughout the day, and especially from day to day even when drawn at the same time. This day to day variation is not well known, and it has only recently been presented by Bowie and associates of the Mayo Clinic.[2] Bowie's results seemed so at variance with classic thinking in the field that James Magidson, chief resident in pathology at Columbia-Presbyterian, with the cooperation of Mrs. Catherine Lang and Mrs. Genevieve Covolo, instituted a blind study of patient and volunteer samples drawn at the same time on different days. The SI in one resting patient was found to vary from a low of 40 ug./100 ml. to a high of 130 ug./100 ml. (older patient with cerebral vascular accident). A normal woman varied from a low of 40 ug./100 ml. to a high of 105 ug./100 ml. when blood was drawn immediately upon awakening and while still in bed. Such variation is far beyond the random variation seen in blind duplicates. The Coefficient of Variation (Standard Deviation expressed as a % of the mean) for blind SI duplicates was ± 3%. In addition to diurnal and day to day variation, SI varies with age and sex. SI falls with increasing age and women are on the average lower than men.

The tremendous variation of SI in normal individuals makes it unwise to place too much reliance on small changes in serum iron. A SI determination without a TIBC determination is practically meaningless (see discussion of examples under Question 2).

The normal range for TIBC is usually given as 300 to 380 ug./100 ml.,[1] but the range will vary with age. For example, at 70 the average value for TIBC is about 250 ug./100 ml. rather than the 340 ug./100 ml. found in young adults. The TIBC is more stable than the SI. For example, the elderly patient whose SI varied from 40 to 130 ug./100 ml. had a TIBC range of from 240 to 310 ug./100 ml. Bowie and associates[2] also found less variation in

TIBC than in SI. Our Coefficient of Variation for TIBC was only ± 3%.

Examples

a. SI 275 and TIBC 285.
Age 50; Sex — Male

The SI is very high and the TIBC is at the lower limit of normal. This could represent hemochromatosis. I have studied four patients with hemochromatosis and all have had SI and TIBC values very close to the values given above. One patient has been followed for 2 years, and his SI and TIBC are still the same despite monthly phlebotomies. In addition to hemochromatosis, however, a similar picture can result from excessive Imferon therapy or severe hemolytic disease.

b. SI 35 and TIBC 410.
Age 30; Sex — Female

The SI is slightly decreased and the TIBC is slightly elevated. The pattern suggests mild iron deficiency. This SI and TIBC pattern is typical of results found in the third trimester of pregnancy. These results are obtained even when patients are on small doses of oral iron.

c. SI 10 and TIBC 180.
Age 25; Sex — Male

The very low SI indicates iron deficiency, which at this age is secondary to blood loss until proven otherwise. However, the very low TIBC indicates serious chronic disease. A serious chronic disease associated with blood loss in this age group is ulcerative colitis. That is what this 25-year-old man had. Similar findings are seen in cases of regional ileitis.

d. SI 10 and TIBC 180.
Age 75; Sex — Male

Again the low SI indicates blood loss, and the very low TIBC indicates serious chronic disease. But this time the patient is 75 years old. The most common serious disease associated with blood loss in this age group is a bleeding neoplasm. This patient had a cancer of the sigmoid colon.

e. SI 10 and TIBC 550.
Age 40: Sex — Female

This is the classic picture of pure iron deficiency anemia. This 40-year-old woman had heavy periods, several children, and took many aspirins. All of these factors tended to deplete her iron stores. In addition, she was found to have an irregular duodenal bulb and was treated for peptic ulcers. With the possible exception of some cases of congenital agammaglobulinemia, a high TIBC means only one thing—iron deficiency. Even after treatment with iron, the high TIBC will persist and make a diagnosis possible.

f. SI 10 and TIBC 380.
Age 85; Sex — Female

The very low SI indicates iron deficiency. The TIBC of 380 is "normal" for a healthy young adult, but is definitely elevated for an 85-year-old patient. This woman had blood loss with an associated rise in TIBC. She was found to have a bleeding duodenal ulcer.

g. SI 210 and TIBC 330.
Age 30; Sex — Female

The SI is elevated and the TIBC is normal. The elevated SI could mean: hemolysis, hepatitis, or very recent therapy with iron. Such a pattern is found, for example, in untreated pernicious anemia. The elevated SI is believed to be secondary to the hemolytic component of untreated PA. The change in SI following treatment with B_{12} is dramatic and diagnostic. Within 12 hours of giving B_{12}, the SI will fall from a level of about 200 ug./100 ml. down to a level of 10 to 30 ug./100 ml. The tremendous drop is believed to be secondary to the sudden increased utilization of iron in the B_{12} deficient patient given a dose of B_{12}.

h. SI 30 and TIBC 165.
Age 50; Sex — Male

The SI is low, but not low enough to be diagnostic of blood loss. The TIBC is very low suggesting serious chronic disease. This pattern is seen frequently in severe chronic uremia or in severe chronic infectious diseases. This patient had uremia.

i. SI 390 and TIBC 330.
Age 40; Sex — Female

The oversaturation seen here is secondary to oral doses of iron in a patient with hepatitis. A similar pattern could be found when unneeded or excess iron is given to a patient with an already elevated SI level. Another common cause is oral iron or recent parenteral iron followed by transfusions of blood.

Summary

Thus, measurement of SI and TIBC remains the best procedure for detection of iron deficiency. The measurement of TIBC is even more important in this regard than the measurement of SI. In addition to diagnostic accuracy, SI and TIBC determinations are harmless, and avoid the unnecessary psychological and physical stress of bone marrow puncture in simple iron deficiency anemia.

R.N.B.

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Metronidazole–A Report Of A Clinical Investigation

Mark Solomkin, M.D. and Stanley W. Edelstein, M.D.

■ The "57" plus varieties of therapy applied to the problem of trichomonas vaginalis is eloquent testimony of the long term ineffectiveness of our present modalities. It has been felt that total effective therapy would include a preparation which would be transported into the deep and recessed hideaways of the flagellate. Until now only the oral preparations promised this capability. However, once introduced, the oral trichomonacides have failed to sustain their curative promise. This is a report of another oral preparation, metronidazole.[1,2] This investigation studied the effectiveness of this drug on 120 women and 16 men.[3] The women were chosen from our private practice. The men were spouses of women who had had trichomonas vaginitis of long standing, or recurrences, or reinfestations.

In the female the diagnosis in every case was made and/or confirmed by the identification of trichomonas on either the wet or the dry smear. The identification having been made, each lady underwent the following work-up:

a) a cbc and blood sedimentation rate at the onset of therapy (and with each course of therapy). This was repeated in two and four weeks;
b) routine urinalyses done at the same times as the blood determinations;
c) superficial neurologic examination looking for changes in reflexes, gait, coordination, equilibrium, and subjective symptoms;
d) follow up wet and/or stained smears after two, four, eight, and twelve weeks.

The men in this study were subjected to the following tests:

a) the cbc, sedimentation rate, and urinalyses as in the female;
b) seminal fluid examination including volume, viscosity, motility of sperm, and percentage of abnormal forms before treatment and six weeks after treatment;
c) urethral and prostatic smears before and at two and four weeks after treatment.

The dosage schedule per course of therapy[4] in women was 750 mgm daily for 10 days. The men received 500 mgm daily for 10 days. This schedule was one which had given previous investigators the "best" results. This schedule was implemented by the administration of sulfisoxazole and phenylazodiaminopyridine HCl[5] to those patients in whom the trichomonas persisted in the urine. This was based on a bit of serendipity. In one patient in whom the trichomonas persisted we also found a bacterial infection. She was given sulfisixazole and phenyl azo-diaminopyridine HCl. Both her infection and the infestation cleared. The persistent bladder infestations thereafter received sulfisoxazole and phenyl azo-diaminopyridine HCl with most excellent results. No attempt was made to study the mode of action of the sulfisoxazole and phenyl azo-diaminopyridine HCl.

Of the 120 women treated with metronidazole, in 105 the vagina was clear after one course of the drug, 15 required a second course of medication, and 13 of this second group (or a total of 118) were found clear. After four months the total "cures" numbered 112. In the remaining eight women there were six relapses plus two women who were never cleared.

Of these 120 women we found a total of 56 harboring trichomonas in the urinary bladder. This was, for us, a surprisingly high percentage. After the first course of metronidazole, 32 still had infested bladders. After the second course, 15 women still had infested bladders. Then the first course of sulfisoxazole and phenyl azo-diamino-

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[1] Metronidazole in the study was supplied as Flagyl by Dr. William Crosson of the G. F. Searle Co.

[2] Physicians Product Brochure No. 69, G. D. Searle & Co., 1963.

[3] The men were studied by Doctors Harold Lear, Walter Schloss, and Bert Berlin.

[4] Perl, G. and Ragazzoni, H., Flagyl in Treatment of "Trichomonas Vaginitis." Obstetrics and Gynecology, May 1962, p. 595.

[5] Trade name Azo-gantrisin. (Roche Laboratories.)

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TABLE I
INFESTATIONS

	VAGINAL			BLADDER		
	NO. OF WOMEN WITH TRICHOMONAS	TOTAL CLEARED NUMBER	TOTAL CLEARED %	NO. OF WOMEN WITH TRICHOMONAS	TOTAL CLEARED NUMBER	TOTAL CLEARED %
Metronidazole						
Onset:	120			56		
1st Course Conclusion:	15	105	87.5	32	24	42.9
Onset:	15			32		
2nd Course Conclusion:	2	118	98.3	15	41	73.2
Sulfisoxazole and Phenyl Azo-Dmnpyrdn						
Onset:				15		
1st Course Conclusion:				2	54	96.4
Onset:				2		
2nd Course Conclusion:				0	56	100
End of study—relapses and not cured	8	112	93.3	0	0	100

TABLE II
HEMOGRAM — FEMALE

	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	16 WEEKS
	1ST	2ND	3RD	4RD	5TH	6TH
Hematocrit	39.9	40.1	42.4	39.9	40.2	39.9
Hemoglobin	12.9	13.0	12.7	12.8	13.1	12.5
w.b.c.[7]	9,200	8,900	8,400	8,100	7,100	8,800
P.	59.7	59.7	58.2	59.2	53.0	58.0
L.	31.1	31.1	32.7	32.2	39.0	33.0
M.	6.9	6.7	6.4	6.7	5.8	6.3
E.	2.1	2.4	2.6	1.9	1.8	2.5
B.	0.2	0.1	0.1	0.1	0.6	0.1
Sed. Rate	21.2	21.7	21.7	22.0	19.0	21.1

pyridine HCl cleared all but two women. The second course cleared the rest.

In the men, the trichomonad was demonstrated in six of the 16 cases. Fourteen wives of the 16 cases were women who had had trichomonas of long standing. In every case when the man was cleared the trichomonad disappeared from the wife.

There were no demonstrated permanent complications in this series. Neurologic examinations looking for changes in reflexes, gait, coordination, and equilibrium were negative. In only one case were the side reactions (ringing in the ears, furry tongue, dizziness, and joint pains) sufficient to cause the patient to stop the drug. As for the rest, the side reactions were minimal and apparently easily controlled by having the patient suck on a "hard candy." Except in the one patient noted, no accurate estimate of the occurrence of side reactions could be obtained because of their subjective nature.

Except for the blood sedimentation rate in the male[6] examination of the blood studies showed no significant changes. The averages are shown in Tables II and III. Because the pages of detail required would serve no useful function and showed no individual case of significant blood changes, the examination of the individual's blood studies which were carried out, are not reported here. In the male we noticed with interest that the average sedimentation rate dropped from 16.1 to 8.0 m.m./hr. after treatment.

The urine studies also showed no significant changes except for the presence or absence of the trichomonas. Attempts to "average, find means," etc. became so detailed that they lacked meaning and so are omitted from this report except to state

TABLE III
HEMOGRAM — MALE

	BEFORE THERAPY	AFTER THERAPY
Hematocrit	45.9	46.6
Hemoglobin	15.2	15.4
w.b.c.[8]	8900	9300
P.	61.9	56.3
L.	27.7	23.0
M.	6.7	7.0
E.	2.9	1.3
B.	0.25	0.0
Sed. Rate	16.1	8.0

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[6] We used Wintrobe Erythrocyte Sedimentation Rate.

[7] The use of averages while illustrating lack of change is not in % as the addition of fractions gave more than 100.

[8] The use of averages while illustrating lack of change is not in % as the addition of fractions gave more than 100.

Table IV

	COUNT	VOL.	PH	ABNORMAL FORMS	2 HRS.	4 HRS.	6 HRS.	8 HRS.	24 HRS.	
Before therapy	140,000,000 per cc	2.9 cc	over 7.5	28.4	64%	56%	44%	33%	15%	45
After therapy	135,000,000 per cc	3.1 cc	over 7.5	27.8	68%	58%	45%	30%	17%	38

that no significant finding other than the presence or absence of the trichomonas was seen.

In the male, semen analysis showed no significant change in sperm count, volume, pH, percentage of abnormal forms, motility, or white cells as noted in Table IV. In every case where the trichomonas was demonstrated, it was eradicated.

Summary And Conclusions

1. Metronidazole is apparently a safe and effective oral trichnomonacide.

2. The urinary bladder was found to harbor the trichomonas in a large percentage of cases and may be one avenue of reinfestation of the vagina.

3. Metronidazole was more effective in clearing the vagina than it was in clearing the urinary bladder. However, the addition of sulfisoxazole and phenyl azo-diaminopyridine HCl quickly cleared the refractory bladder with no recurrences or reinfestations during the period studied.

4. The simultaneous treatment of 16 males with Metronidazole resulted in the eradication of the recurrence of trichomonas in 14 spouses who were known to have been afflicted with trichomonas vaginitis for a long time.

5. The trichomonad was demonstrated in six of 16 males studied. In every case they were eradicated by a single course of metronidazole.

6. Except for a drop in the sedimentation rate in the male, no significant neurologic, blood, or urinary changes were found in either men or women. There were no significant changes in the semen.

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Sites Of Intestinal Absorption

Richard P. Spencer, M.D.

■ The most obvious gross characteristic of the small intestine is its length. Certain advantages of this length can be appreciated. For example, the small intestine, which is about three times the linear dimension of its host, provides a large surface area for absorption. In addition, the length allows for greater time of contact between nutrients and the absorptive surface. There is, however, more to this story than just these superficial thoughts. The striking fact is that the activities of the small intestine are not distributed uniformly down the length of the gut. This has interesting clinical implications, as will be pointed out shortly.

A stimulus for such studies have been in vitro experiments on isolated intestinal sacs.[1] These sacs transport certain carbohydrates and amino acids against a concentration gradient. Each of these absorptive events has its own particular spatial distribution.[2] For example, in most species the intestinal absorption of glucose decreases linearly as the distance from the pyloric valve increases. All of the amino acids which are transported by in vitro hamster intestinal preparations, however, are maximally absorbed at a point about 80 per cent of the way down the small gut.[3] This result with amino acids is rather interesting, since we know clinically that most of the amino acids are absorbed before the first one-third of the small intestine is passed. What, then, is the significance of the in vitro distribution pattern? Perhaps this indicates that there is a far greater absorptive ability for amino acids than is normally called upon. Hence, if the upper one-third of the intestine were damaged, or surgically removed, there might be little or no difficulty in absorbing amino acids lower down. This likely is true, for defects of amino acid absorption, other than congenital defects, appear to be exceedingly rare. That is, malabsorbing individuals may have defects of fat absorption and of carbohydrate absorption, but acquired defects of amino acid absorption per se have not been clearly pointed out.

Not only absorptive abilities, but also enzyme activities, are distributed non-uniformly down the length of the small gut. The full significance of this in terms of the interrelationship of motility, digestion, and absorption has not yet begun to be appreciated. In some cases, these interrelations may be quite complex. Take, for example, the absorption of fats. An experimental approach to determining which area is involved in absorption is to surgically remove part of the small gut and allow the animal to recover. Following recovery the nutrient can be fed and absorption followed, either by disappearance from the lumen or appearance in the blood stream. Results with lipids and cholesterol absorption were anomalous. Some reports stated that removal of the upper portion of the small intestine resulted in malabsorption of lipids. Other investigators, however, concluded that removal of the lower one-third of the small gut resulted in lipid malabsorption. The clue to what was occurring was provided by experiments which fed large quantities of bile salts with the lipids. When bile salts were fed, absorption was normal even though the final one-third of the small gut had been removed. The eventual solution to the problem was as follows. Apparently bile salts themselves are reabsorbed from the small intestine.[4] This appears to be a process which occurs almost entirely in the lower one-third of the small gut. This can be shown very nicely in vitro in which some of these compounds move against a concentration gradient. When the lower one-third of the small gut is removed there is bile salt wastage, at least in most animal species. The normal reabsorption of bile salts (via entry into the lymphatics and blood stream and thence to the liver), is prevented when the lower one-third of the small gut is removed. There is then wastage of the bile salts, improper emulsification of lipids, and hence lipid malabsorption. It appears now that the body can absorb lipids at almost any level. In some species this occurs quite well in the upper one-third of the gut. However, the entire process is dependent upon the presence of bile salts. This case illustrates the fact that when we are studying the absorption of one moiety, we must be aware that there are other operative factors. When we remove a piece of small gut to study absorption we are also removing cer-

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tain digestive enzymes; we are also altering motility.

There is also another experimental approach possible in order to determine the site of intestinal absorption. This involves not removal of the segment, but rather its transposition from one locale to another. For example, surgical transposition of the ileum can be accomplished in dogs. The ileum is removed from its normal locale adjacent to the cecum and is transposed between the duodenum and jejunum.[5] With this in mind, first let us examine vitamin B_{12} absorption in the normal small intestine of a dog. The technique is to administer vitamin B_{12} labeled with radioactive cobalt, in this case Co^{60}, as well as intrinsic factor. Following such administration, the vitamin is absorbed from the lumen into the gut wall. It is found that the vitamin passes from the gut lumen into the intestinal wall and is "hung up" intramurally for several hours before it enters the blood stream in appreciable amounts. The dogs were sacrificed, the small gut was then flushed through with saline, and segments were counted. In unoperated, and control operated dogs, vitamin B_{12} absorption occurred entirely in the ileum.

When the experiments were performed after half of the ileum had been transposed between duodenum and jejunum, it was observed that there were two peaks of absorption. One occurred in the transposed half ileum and one in the normally placed remaining half ileum. In still other dogs the entire ileum was transposed between duodenum and jejunum, and the dogs were allowed to recover. All the vitamin B_{12} absorption then occurred in the transposed ileal segment. There was no evidence that any other part of the gut absorbed the vitamin at these low concentrations (that is, on the order of 0.5 to 1 microgram). If larger quantities of the vitamin are given, that is massive amounts on the order of hundreds or thousands of micrograms, then some small quantity passes by diffusion. However, in physiological concentrations, absorption of vitamin B_{12} is entirely a function of the ileum.

When the ileum was removed, there was no absorption of vitamin B_{12} in the dog. To the best of our knowledge, there has been no adaptation of these dogs for a period of about one year. That is, other sections of the small gut did not adapt to absorb vitamin B_{12} at these low concentrations. The result here appears to be clear-cut. It is, indeed, one of the few clear-cut biological experiments on transport. Vitamin B_{12} absorption at low concentrations is a function of the ileum and when the ileum is transposed, B_{12} absorption still occurs in the transposed ileal loop. Can such observations be used to alter absorption? Some surgical groups have utilized removal of the ileum. If the ileum were removed there would certainly be decreased absorption of fats because there would be massive loss of bile salts. There would, however, be other difficulties. Vitamin B_{12} absorption would not occur if the ileum had been removed. If it were left as a blind loop, it would not be in continuity with the major part of the small gut. Vitamin B_{12} absorption would not occur and one would also have difficulty with a so-called "blind loop syndrome." Hence, attempts to surgically remove parts of the small gut to alter absorption are still in their early and very uncertain state.

There is also another intriguing possibility. This is to remove a section of the small intestine and turn it in an antiperistaltic fashion, and then reanastamose the segment. If the reversed segment were too long there would be no passage of food materials through the region and the animal would die, eventually, of starvation. If the section is small enough, however, there may be food passage and the total time of transit would be somewhat prolonged. This has been reported as being of some use in patients who suffer from very short intestinal transit times. Precisely what happens to the absorptive capacities of this reverse segment has not yet been documented.

These are only some early observations on studies of the sites of intestinal absorption, and attempts to alter these through surgical intervention. Studies are needed to determine if the sites of intestinal absorption vary with age and with disease states. Clinical data are required to help define the absorptive areas for each nutrient, in normal individuals and in those with various gastrointestinal disorders. There are two principal ways in which this can be accomplished clinically.

1. By use of intestinal biopsy specimens. The site of intestinal biopsies, taken via the peroral route, can be described in terms of the length of tubing swallowed. Not only can the tissue so removed be studied for its microscopic appearance, it can be utilized for investigations of both enzyme content and obsorptive capacity.[6] Hence, it is possible to correlate histology, enzyme content, and absorptive ability with distance down the small intestine.
2. By studies before and after intestinal surgery. When a section of small intestine is removed surgically it is essential not only to specify the length extirpated, but also the site of removal. Ablation of 20 cm. of ileum may be a far greater insult to absorption than removal of an equal length of midgut. If possible, absorptive studies before and after small bowel surgery are to be recommended if accurate data are to be complied as to the effects of intestinal removal on absorption.

By way of summary, three points can be made:

1. Some absorptive events are site specific, and there is decreased uptake if the area is damaged or removed (example: ileal absorption of vitamin B_{12}).
2. Still other absorptive processes in the small intestine depend upon the functioning of distant regions. Examples:
    a. Vitamin B_{12} absorption from the ileum depends upon intrinsic factor, which is produced in the stomach.
    b. Lipid absorption in the first two-thirds of the small bowel depends upon bile salts (which themselves are absorbed in the distal one-third of the gut).
3. The majority of absorptive events (amino acids are an example) have a great "overabundance" of surface area and transport capacity; removal of one region does not result in malabsorption of the metabolite.

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Observation And Experiment In The Medical Sciences

The state of inorganic chemistry in the early nineties of the last century showed some traces of the conditions which too exclusive a reverence for experiment is apt to bring about. The inspiration of the atomic idea was manifestly dying, yet any whisper that the atom might not be the ultimate unit of reality was apt to be snubbed as speculative and unscientific. Nevertheless this impeccable science could tolerate for many years a discrepancy of the order of one percent in the results of the different methods of preparing nitrogen, and with all its faith in experiment could ascribe the discrepancy to experimental error. And all the while, behind the meagre veil of this experimental error the inert gases of the air were impatiently awaiting discovery. The agitated scepticism with which the discovery of argon was received, no less than the great growth of which that discovery was the germ, illustrated how much chemistry had for the moment lost the aptitude for new ideas and the elasticity of mind which their currency produces.—*The Collected Papers of Wilfred Trotter, F.R.S. London, Oxford, University Press,* 1946 p. 122.

Allergy And Chronic Simple Glaucoma

Louis F. Raymond, M.D.

■ Woods,[1] Berens,[2] Duggan,[3] and others have shown the eye to be susceptible to food and other forms of hypersensitivity, as manifested by various forms of acute inflammatory responses. Although clinically there are numerous reported instances in which allergy (hypersensitivity) was found accompanying an eye disorder, there is little clinical, and practically no experimental evidence to adequately implicate the allergic mechanism as the underlying cause of chronic simple glaucoma. Rycroft,[4] Friedenwald,[5] and others have suggested that histamine may produce glaucoma. Sjorgen,[6] Weekers et al[7] and Kraupa,[8] have discussed the role of an allergic etiology in glaucoma.

Among Koch's postulates is included the statement to the effect that in order to prove the etology of a contagious disease, one must be able to produce the original disease. I have applied this approach on numerous occasions and produced or exacerbated symptoms of glaucoma during treatment of patients afflicted with this ocular disorder.

Chronic simple glaucoma is not an isolated eye disease but an immunologic disease with eye manifestations which are characterized by congestion and edema.

Exacerbation of glaucoma in humans and control is illustrated by the following:

Case History Number 1

A 40-year old white male, when first seen, presented the classical picture of early chronic simple glaucoma with normal visual fields. He was treated with miotics. The intraocular pressure under treatment was 16 mm Schiotz (S). The patient was tested for allergies by the intradermal injection of several of the more commonly known offending antigens. After the injection of one particular antigen, he developed a well-defined wheal, indicating a strong, positive reaction; his intraocular tensions were measured at this time and recorded at 34 mm (S) in both eyes. In addtion, the patient experienced the same symptoms which initially led him to seek medical advice, i.e. he complained of blurred vision. This visual impairment, therapeutically induced, cleared shortly after the intravenous injection of calcium gluconate and an antihistamine, (promethazine hydrochloride*). Eight minutes later the pressure returned to the initial level of 16 mm (S).

This clinical demonstration illustrated that it is possible to reproduce the same signs and symptoms of chronic simple glaucoma in the same patient by eliciting an allergic response in an already sensitized patient and then, by treating the patient with an antagonist—in this case an antihistamine—obtain clinical remission.

An example of an immediate type of hypersensitivity response:

Case History Number 2

A 32-year old colored male with the chief complaint of blurred vision in the right eye with colors or halos around lights of four days' duration. Patient stated the same episode happened one year previously in the left eye.

Inquiry revealed that one year previously he was treated for chronic simple glaucoma at one of our well-known teaching eye clinics. He still had in his possession the medication given him at that time, pilocarpine 1%. Examination revealed intraocular tension in the right eye 47 mm (S) and in the left eye 16 mm (S). The visual field showed; the presence of an enlarged blind spot in the right eye, the left eye was normal.

Instillation of pilocarpine in the office did not change the vision or the tension after three hours. He was tested with a seasonal mixed pollen for sensitivity. Four hours later his test became positive, his vision cleared and the intraocular tension reverted to normal 16 mm (S) in both eyes. Two days later all local eye medication was discontinued, the vision remained clear. Central vision uncorrected in each eye was 20/20. The intraocular tension was 10 mm (S) in each eye. Desensitization treatment was given: all the usual eye findings were normal in one week: vision, visual fields and tension. Normal findings are still present, without any other treatment systemically, or locally to the eye, except for hyposensitization. This is an example of delayed type of hypersensitivity.

Post operative type of chronic simple glaucoma with symptoms and progressive loss of vision were reversed as illustrated by case history number three:

Case History Number 3

An elderly woman, who two years previously, had surgery performed for bilateral glaucoma. Surgery consisted of an iridencleisis in the right eye and a peripheral iridectomy in the left eye. She was first seen by me in August, 1961—her chief complaint was: "I see halos around lights." The intraocular tension was measured and found to be normal—16 mm (S), in both eyes. Examination with the slit lamp revealed a shallow anterior chamber with apparent adequate drainage as confirmed by goniscopic examination. The visual fields were normal. Because of the normal tension, the patient was

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* R Phenergan—Wyeth Laboratories.

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not treated with miotics or carbonic anhydrase inhibitors.

It was noted from her case history that her initial acute attack of glaucoma occurred in the fall of the previous year. At that time she required bilateral surgery. About a year later, also in the fall, the patient re-experienced subjective symptoms of glaucoma, i.e. halos around lights. Since the attacks occurred in the fall (pollen season) the patient was suspected of having an allergy, was tested and found to have sensitivity to pollen. Within two weeks after starting the desensitization treatment, the patient's halos disappeared; the chambers which were originally shallow now were deeper and better defined.

The patient maintained normal intraocular tension throughout the course of treatment. The chambers remained deep and well defined; the central vision was normal. Treatment was stopped, and on several subsequent visits the patient complained of halos and stated that she had reduction in visual acuity. At this time it was noted that the chambers were shallow in both eyes. Initially, the central vision was uncorrected—20/60 in the right eye and 20/40 in the left eye. After treatment, for four additional weeks, the uncorrected vision in each eye improved to 20/20. The patient has maintained 20/20 vision and reported at weekly intervals for desensitization treatment. She now requires no treatment.

This case is included to illustrate a point, i.e. although surgical drainage is well established, signs of glaucoma may persist unless treated on a specific etiologic basis, to give complete remission of all visual symptoms.

Discussion

Chronic simple glaucoma is usually considered to be a localized eye disease. The clinical histopathological evidence strongly suggests that it is a generalized systemic disease, immunologic in nature and accompanied with various eye manifestations. Chronic simple glaucoma is therefore not a single disease, but may be an allergic disease with eye manifestations. It can be induced by sensitization and cleared by hyposensitization, this has been done clinically upon humans on repeated occasions.

It is possible under proper allergic diagnosis and management to control intraocular tension, correct visual field defect in early cases, reduce congestion and edema and to correct subjective glaucoma symptoms and improve vision in the early stages of the disease.

Grossly the symptoms most readily identified in any person suffering with an allergy are associated with some form of congestion and edema. These same responses were found by McCombs et al[9] and Sabesin.[10] McKay[11] et al and Rider[12] have shown severe systemic pathologic changes associated with hypersensitivity. Exposure of sensitized individuals to an offending allergen in most instances does not precipitate an attack of chronic simple glaucoma although edema and inflammation of ocular tissues are probably present to some degree in all. Further, in some of these individuals, visual changes are undoubtedly present but may not be sufficiently severe to be readily apparent.

At the present time, it appears that the clinical and experimental evidence validates the observations of Sjogren,[13] Weekers,[14] and Kraupa[15] that allergy may be responsible for some cases of chronic simple glaucoma. Early diagnosis together with specific desensitization therapy may offer glaucoma patients a more favorable prognosis.

Conclusion

Clinical evidence is presented in three cases to illustrate that chronic simple glaucoma is not an isolated local eye disease, but may be a systemic disease sometimes immunologic in nature. Chronic simple glaucoma may be cured in its early stages by specific therapy based on allergic diagnosis and treatment.

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Roentgen Diagnosis Of Gallstone Ileus

Joseph J. Esposito, M.D.

■ Gall stone ileus or cholelithic obturation are terms applied to intestinal obstruction caused by the impaction of a gall stone in the intestine. Its incidence in the reports of larger series is estimated at one per cent to two per cent of causes of mechanical obstruction.[1–5] Predominantly females are afflicted and in particular elderly patients. Thus in agreement with other reports,[4,5] in our series of fifteen patients, ages ranged from 60 to 81 years. The fact that this is essentially a disease of old age undoubtedly contributes, at least in part, to the high mortality. The surgical mortality again varies according to reports for an estimated average of about 25 per cent[6] but ranging as high as 47 per cent.[2,5] There also appears to be a direct relationship between earlier operability and improved mortality.[1] Since this condition does represent a potentially serious clinical situation, any procedure presenting a reasonably accurate pre-operative diagnosis is important. A review of fifteen cases of gall stone ileus will serve to indicate that roentgenographic examination provides such a major diagnostic aid.

The roentgen signs of a gall stone ileus are: 1. air in the biliary system; (Figure I) 2. visible calculus in the intestinal tract; 3. the demonstrable migration of a calculus over serial or interval examinations. (Figures IIa, b) The term gall stone ileus implies the necessary demonstration of evidence of intestinal obstruction. In other words, one is confronted with the case of intestinal ileus and then must find one or more of these additional findings to indicate that the cause of the ileus is an impacted gall stone. This seemingly elementary remark seems warranted since some of the recent literature has indicated that the presence of small intestinal fluid levels, as the only roentgen sign, constitutes sufficient basis for the diagnosis. This, of course, is a presumptive diagnosis in those cases of intestinal ileus in elderly women who have an antecedent history of gall bladder disease and no other apparent reason for the obstruction.[1–5] Perhaps more justifiable is the demonstration of a changing level of intestinal ileus to indicate that

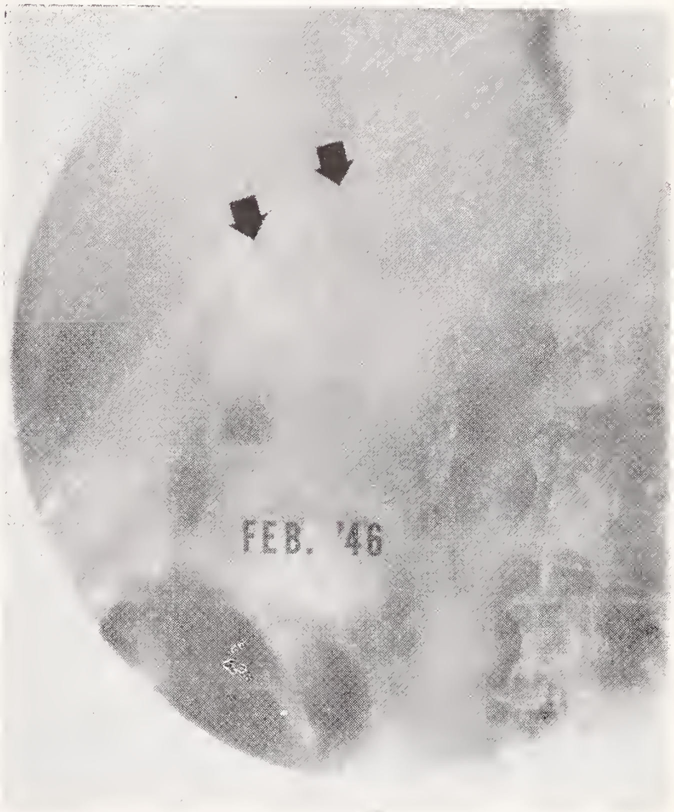

Figure II A
Radiographic examination of gall bladder area of 66-year-old female with mild upper abdominal pain showing two large calcific gallstones. No surgery was done.

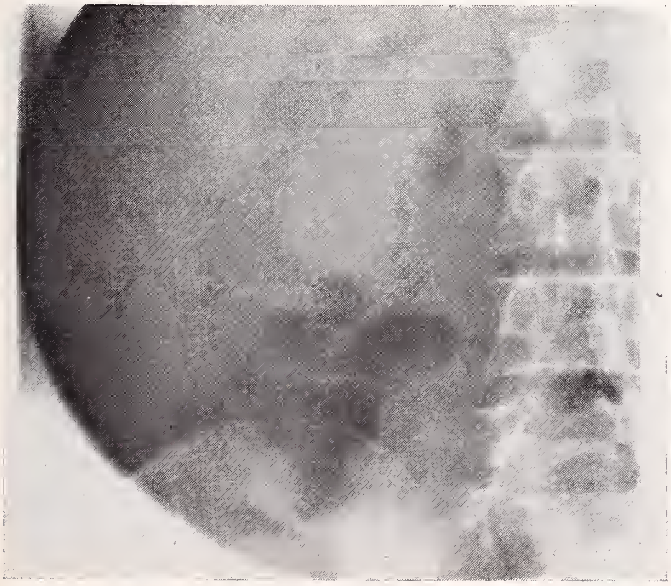

Figure I
The radiographic appearance of air in the biliary system, the almost pathognomic roentgen sign of gall stone ileus.

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the obstructive process is migrating in nature. We would definitely agree that, as in many other diagnostic problems, the awareness of the possibility of the diagnosis is a strong factor in making it. These statements are in reference to the plain roentgenograms of the abdomen. There are, of course, further diagnostic procedures such as the use of barium or other opaque intestinal media in the presence of an intestinal obstruction in which case the opaque medium may fortunately outline the oval contour typical of intestinal calculus.[9] (Figures III, IV)

We have reviewed fifteen cases of gall stone ileus and Table I represents a tabulation of the findings. It is notable that air in the biliary system and visible calculus are the prime diagnostic signs. Each of these was present in six cases although in only one case were they present together.

Discussion

By far, the most common route by which a gall stone migrates into the intestinal tract is by way of an internal biliary fistula.[1] Necrosis of the gall bladder fundus with communication through to the duodenum (or any other gastro-intestinal lumen) permits the passage of a calculus which then may migrate, gradually increasing in size so as to cause impaction usually lower in the intestinal tract. It is true, however, that the migration of a calculus through an intact biliary system can occur. Many experienced radiologists have encountered instances in which the surgeon reports either no calculi or less calculi than observed on a pre-operative cholecystogram, in which it is evident that calculi have in the interval progressed through the cystic duct, common duct, and into the duodenum. There is little doubt in this author's mind that so-called spontaneous disappearance of gall bladder calculi is most often accounted for by this migration.[7,8] Further, not all cases of enteric calculi cause obstruction. It is estimated that actually less than half of these result in clinical or significant intestinal obstruction.[1]

TABLE I
RADIOGRAPHIC FINDINGS

PT.	AGE	SEX	AIR BILIARY SYSTEM	VISIBLE CALCULUS	ILEUS	LOCATION CALCULUS	PRE-OP DX MADE
1. L.D.	62	F	0	+	+	Colon	+
2. M.C.	76	F	0	+	+	Ileum	+
3. E.C.	80	F	0	+	+	Ileum	+
4. E.P.	71	F	+	0	+	Ileum	+
5. G.G.	60	F	0	+	+	Colon	+
6. M.B.	66	F	+	+	+	Ileum	+
7. T.S.	66	F	0	0	+	Ileum	0
8. S.P.	68	M	0	0	+	Ileum	0
9. E.B.	66	F	0	0	+	Ileum	0
10. G.M.	70	F	0	+	+	Jejunum	+
11. G.B.	76	M	+	0	+	Ileocecal	+
12. E.V.	80	F	+	0	+	Jejunum	+
13. R.G.	69	F	+	0	+	Ileocecal	+
14. M.P.	81	M	+	0	+	Ileum	+
15. M.B.	74	F	0	0	+	Ileum	0
Total 15		F, 12; M, 3	6	6	15		11

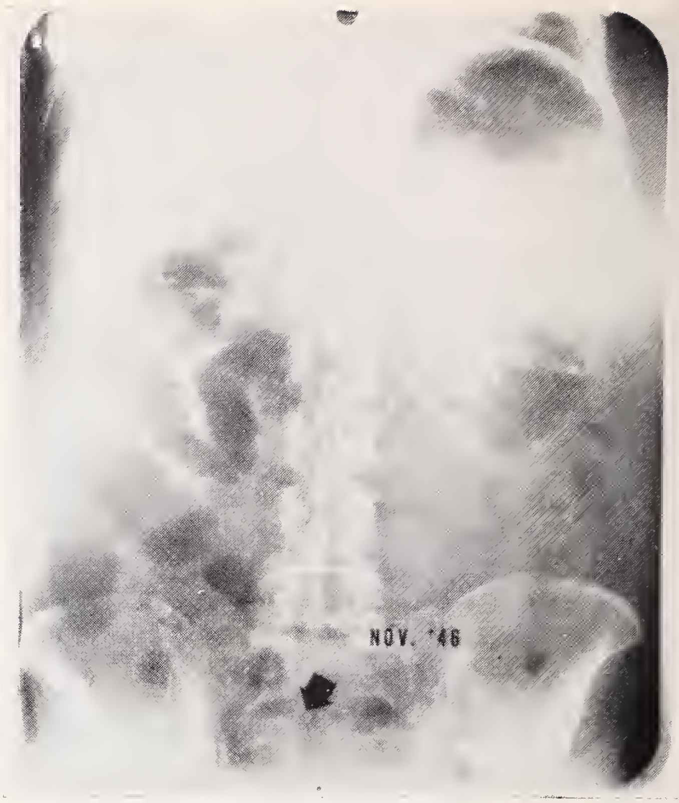

FIGURE II B
Same case as 2A several months later. Now presents symptoms of intestinal obstruction. There is only one calculus in the right upper abdomen. The second is seen in the lower abdomen. Note that this single patient presents all the roentgen signs; air in biliary system, visible calculus, migration of a calculus, ileus.

Air in the biliary system is an almost pathognomic roentgen sign of gallstone ileus. It has been found in six of our fifteen cases. It is true that there are other causes, however, for air in the biliary system. An internal biliary duodenal fistula not associated with the passage of calculi may, by reflux, present air in the biliary system. At this point, one might again emphasize that while an internal biliary fistula may be accompanied by gall stone ileus, this is not necessarily universal. There are many cases of internal fistula not associated with calculi and conversely there are some fewer cases of gall stone ileus which are not accompanied by internal biliary fistula.[3] Other causes for air in the biliary system include acute emphysematous cholecystitis and reflux secondary to surgical procedure, e.g., sphincterotomy. Thus, when there is no visible calculus, the presence of air in the biliary system in association with a reflex

Table II

LOCATION OF STONE			(BROCKIS)	(KIRKLAND)
Ileum	11	73%	72%	66%
Jejunum	2	13%	17%	24%
Other	2	13%	11%	10%

or adynamic-type of ileus in the intestinal tract may lead to difficulty in diagnosis.

The review of our cases indicates that the most common site of calculus impaction is the terminal ileum. This agrees with the findings of other reviews.[1,3,4,5] This probably occurs because of a gradually enlarging calculus migrating into the decreasing caliber of the lumen of the terminal ileum, further affected by the presence of the weaker peristalsis in this portion of the intestine. Table II compares our findings with other reviews.

The size of the calculus is also of importance. It is sometimes difficult to exactly correlate the size of the roentgen image with the pathological specimen but it would appear that in most instances an obstructing calculus is at least, or close to, 3 cm. in size.[1] The surface apposition of non-radio opaque material, of course, would render a calculus larger than the calcific roentgen image. The shape of the calculus may have some significance. It is probable that the calculus with sharp or irregular edges would be more likely to cause regional intestinal spasm and could be comparatively impaired in motility.

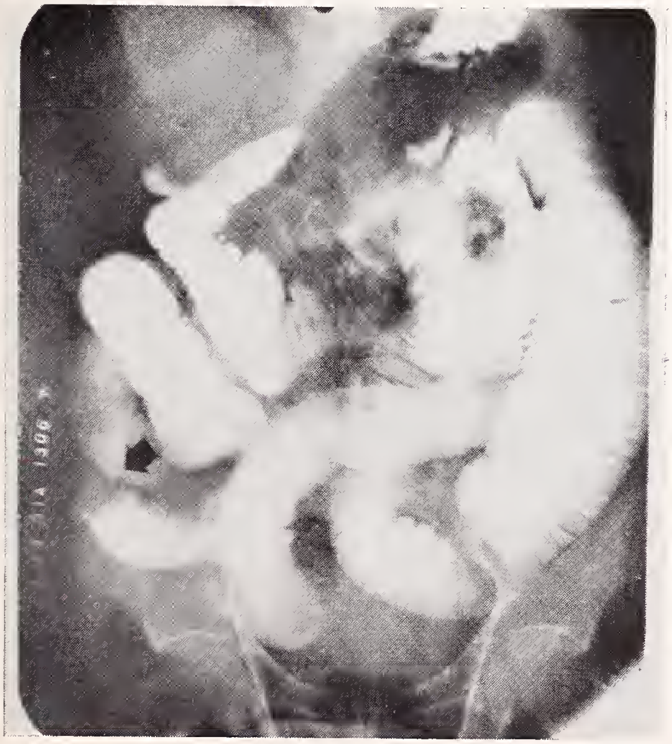

Figure III

Eighty-one year old male, barium outlines dilated obstructed loops of small intestine and delineates oval radiolucency indicating calculus. At surgery, a 3 cm. diameter calculus found in lower ileum.

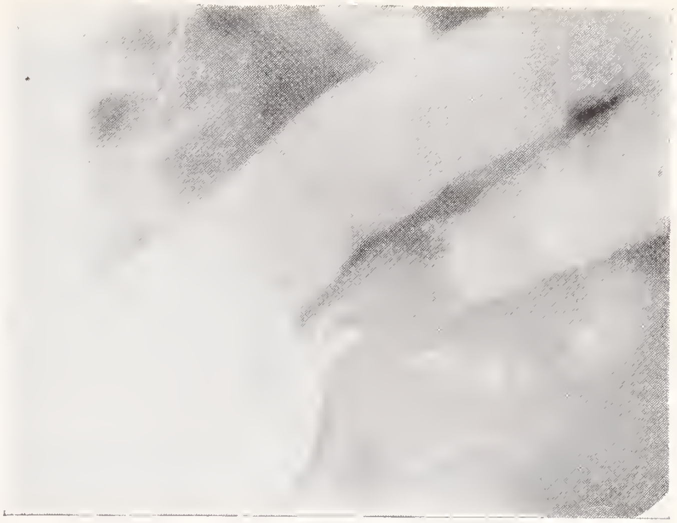

Figure IV

Sixty-year old female, barium enema examination outlines gallstone in proximal sigmoid colon.

The correct pre-operative diagnosis of gall stone ileus has been reported variously in the different reviews. Raiford, for example, reports in his series 51.7 per cent correct pre-operative diagnosis; Buetow reports an incidence of 48 per cent; Kirkland 83 per cent. It is significant that the most recent reviews of gall stone ileus show improvement in both the diagnostic accuracy and in surgical mortality. In our series, the diagnosis was made pre-operatively in 11 of the 15 cases, for a 73.3 per cent. One must stress the important role played by technique in these elderly and usually quiet ill patients. Conditions are not always favorable for optimum roentgenographic technique. There is no doubt that the awareness of the possibility of the clinical diagnosis would greatly enhance the diagnostic yield roentgenographically.

Summary

The roentgen diagnosis of gall stone ileus with a review of 15 cases has been presented. The findings indicate that the roentgen diagnosis of this condition is a significantly reliable and accurate one and that the diagnosis can be made pre-operatively in a large number of cases.

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Aneurysm

Among the diseases of the cardiovascular system aneurysm stands out as having by its obvious features forced due recognition long before the circulation was discovered, thus contrasting with cardiac disease which up to the eighteenth century was thought not to occur. Antyllos (A.D. 55-118) operated upon it, and Galen (A.D. 130-200) described two forms, the traumatic and spontaneous. The traumatic and superficial aneurysm was that mainly seen until syphilis became widespread after the return in 1493 of Columbus from the New World and the occupation of Naples by the army of Charles VIII in 1495; there was then what has been called an unprecedented occurrence of aortic aneurysm. The association with syphilis did not escape Fernelius who in 1542 first recognized internal aneurysms, Vesalius who about 1557 diagnosed both thoracic and abdominal aneurysms, and Ambroise Paré (1582) who incriminated mercurial treatment as a cause of aneurysm . . .

Early in this century the Wassermann reaction (1906) facilitated the detection of clinically latent syphilis, and early changes in and around the vasa vasorum of the aorta (mesaortitis, Heller) and the presence there of the *Spironema pallidum* (Schaudinn and Hoffmann, 1905) fully established the paramount importance of syphilis in the etiological relationship of aneurysm . . .

In aneurysm, particularly intrathoracic, though syphilis is in the vast number of instances the important underlying factor, the influence of strain as an immediate exciting cause must not be overlooked; further, in some instances, luetic infection is not concerned: in old people dissecting aneurysms and abdominal aneurysms may be due to ordinary arteriosclerosis.—Sir Humphrey Davy Rolleston. *The Harveian Oration.* Great Britain, Cambridge University Press 1928, p. 56.

On The Tongue Of Our Craft

Marcus Backer, M.D.

■ More than many another medium of communication medical language everywhere borrows much from antiquity. Our terminology taps the wells of Latin and Greek as avidly in Tashkent as in Rome, Stockholm, or Addis Ababa.

Here and there, even Greek mythology lends us a helping hand. We single out slender fingers from among all other findings in Marfan's syndrome and call them arachnodactyly. In the background is the legend of a skillful girl who riled the goddess Athene. The angered goddess, jealous of the girl's artistic perfection, changed her into a spider, arachne. In our aim to stress the long limbs in this disease we did not christen it "daddy long-leg" syndrome, but we did give Athene's mean trick a place in Marfan's syndrome.

An old Theban saga helps us diagnose the Oedipus complex. And Venus herself not only shares our anatomical homage to the imposing mons Veneris of the female; she also labels the disenchantment of venereal disease. After Priapus, the god of procreation, we dignify a painful and not so procreative state in the male. Conversely, the ever-sharp female with an intensely amorous obsession may thank the youthful Greek nymphs for the name of her special mania.

Lest it wrongly appear as if our language favors pagan gods and their not always decorous consorts, here are some examples of our professional kinship not with sinners but with saints of record. Chorea is linked with no less than three saints: Saint Vitus' dance; Saint Guy's dance; Saint Anthony's dance. Saint Anthony's fire are the flaming words for erysipelas, while the prosaic Saint Blaize's disease denotes the same as quinsy. In the mouth cavity again, the high sounding Saint Apollonia's disease is just a tooth-ache. Among other illnesses named after saints, epilepsy is Saint Valentine's disease, bubonic plague is Saint Roche's disease, pellagra is Saint Ignatius' itch.

Would any one still accuse our tongue of stunted growth, meager heritage, or scant versatility? If so, one may find our craft on some imaginative excursions into the animal Kingdom, the botanical world, the outer space, and other places. We describe a hare-lip just as the Germans call it "Hasenscharte." We look at elephantiasis, ichthyosis, buffalo-humps, and moon-faces. We see strawberry-tongues, we feel a water-hammer pulse, and we hear pistol-shot sounds and crescendo murmurs.

Very few illnesses, though, let us join old grandmother in her own time-honored tongue. We do spare her pertussis, rubella, and hemorrhoids, and talk to her of whooping cough, measles, and piles.

Occasionally, we combine several words in order to better define a pathological entity. Then we may draw upon both Latin and Greek, as in subacute, disseminated lupus erythematosus. Here, the first three words are taken from Latin, the fourth stems from Greek. The trouble often encountered in such instances is the wrong genders of the adjectives or some such monstrosity in print as lupus "erythematosis," with an i, of all things. By no means rare in medical literature is the previously[1] mentioned lupus "erythematosus, disseminata," with one adjective in the masculine and the other in the feminine gender. Still, lupus, the wolf, is not hermaphroditic.

A disastrous blunder was found recently on one of the University of Miami buildings. An attempt at stating the year of its erection in Latin used the word "ano," in the anus, instead of anno, in the year. Such a spectacle brings back the old question why those "poorly versed in Latin do not stop using it and write English."[1]

The suffix "-itis" is accepted as denoting inflammation or infection: rhinitis; hepatits. But we are not always consistent about this. For example, we adhere to the Greek word "hepar" meaning liver for its derivative hepatitis. But we ignore the Latin vertebra and coin "spondylitis" from "spondylos," the Greek term for vertebra. We would not have the spine suffer from vertebritis, only from spondylitis.

With universal consensus our profession embraces the Latin title of doctor for its membership. Soon after the graduation honeymoon we learn that the road is endless, and that we need sobriety, humility, and labor, not a titular badge of learnedness. To the ancient Greeks the physician was "hiathros," healer, a title honorable enough; to the old Romans, he was simply "medicus."

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Distinctions other than "doctor" adopted from Latin and Greek do serve a useful purpose in specifying our various fields of endeavor. For what else might we say with ease instead of anatomist, embryologist, proctologist? Interestingly, the Germans, as often as not, refer to the "Augenarzt," eye physician; "Kinderarzt," children's physician; "Frauenarzt," women's physician; "Zahnarzt," dentist. They also speak of "Haarausfall" for alopecia, "Lungenentzündung" for pneumonia, "Vorsteherdrüse" for prostate, "Beschneidung" for circumcision. In all these and similar instances they speak unadulterated German, without recourse to Latin or Greek.

When we refer in our own publications to medical sources from Switzerland, Austria, or Germany, the language of the bibliography is often shockingly incorrect. One wonders how dependably authors manage to peruse the papers they quote, when the errors in their references betray but poor acquaintance with the foreign tongue.

* * * * *

Now, how articulate is our English ken in medical writings and at conference tables? Here follow some examples of a blemish or two on our literary face:

Young and old speakers and writers keep repeating: "Physical examination revealed that the patient . . ." or "physical examination disclosed that the patient . . ." Why not state the findings directly? What is wrong with saying: "The patient was pale and had petechial spots on the abdomen?" Of course, the "revelations" and "disclosures" were made on examination, not at the oracle of Delphi.

The word "there" is repeated ad nauseam in medical reports. A roentgenologist writes in one and the same opinion: "There is no evidence of atelectasis, . . . there is no hilar lymphadenopathy, . . . there is left ventricular hypertrophy, . . . there is no evidence of mucosal ulceration of the colon, there is a moderate amount of feces within the cecum, . . . there is an elongation of the sigmoid." Really, hadn't one better say: No atelectasis and no hilar lymphadenopathy were found, . . . the left ventricle is enlarged, . . . the mucosa of the colon is not ulcerated, . . . the cecum contains a moderate amount of feces, . . . the sigmoid is elongated.

In the J.A.M.A. appears a publication under the heading "Diagnosis and Treatment of Cardiac Pericarditis," as if pericarditis of any other kind were possible.

Recently, someone has defined vertigo as a "hallucination of motion." In any language, hallucination is a psychiatric symptom. Vertigo, to be sure, has no psychiatric significance, per se. It might be defined correctly as an illusion of motion.

Futile and meaningless are two words which we occasionally employ when we don't know any better: essential, and idiopathic. For instance, we should long since have abandoned the term essential hypertension. That type of hypertension whose exact pathogenesis as yet resists recognition might better just continue to be called familial hypertension. At least, familial occurrence is incomparably more predominant in this hypertensive state than in other forms of hypertensive disease.

Last but not least, the English in our journals is bloated with verbose redundancy at times. A renowned clinician writes in the *Annals of Internal Medicine*: "Numerous other rare types of heart disease can be enumerated which need to be considered when one is presented with cases that do not fall readily into the more common groups." Briefly, and no less lucidly one might say: "Numerous other rare types of heart disease not readily placed in the more common groups need consideration." Seventeen instead of thirty-one words state exactly the same thing.

That master of the English tongue who in the last World War promised Britain "blood, toil, tears, and sweat" was brief, terse, and incisive. So was Titus upon his triumphant return to Rome. He said laconically: "Veni, vidi, vici." I came, saw, and conquered. Medicine should at least not be going to the opposite extreme, and it should grind its linguistic tools to a keen edge.

Reference

1. Backer, M.: Caveat Scriptor. New Engl. J. Med., 259: 1125, 1958.

FROM THE GENERAL MANAGER'S OFFICE

William R. Richards, m.d., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, September 10, 1964

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gilman, Cullen O'Connor, Goldberg, Weise, Sr., Pitock, Bradley, Grendon, Caplan, Ayres, Rogol, Ciccarelli, Seigle, Fabro, Abbot, Egan, W. Martin, and Major. Also present were: Mrs. Lindquist, Mr. Burch and Dr. Richards. Absent were: Drs. Hess, Brandon, Davis, Gardner, Grant, Phillips, Hughes, Shepard, Spitz, and Hastings.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of July 15, 1964.

Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members:

Albert J. Howard, New Haven (NHCMA–1964
Lillian C. Warnshuis, New London (NLCMA)

CSMS Dues Exemptions

It was VOTED to grant exemption from payment of CSMS annual dues to the following, for the reason and period indicated:

Franklin H. Epstein, New Haven (NHCMA)—Postgraduate Education

Resignation—Joint Conference Committee With CPA

It was VOTED to accept the resignation of Dana L. Blanchard, Branford, as a member of the Joint Conference Committee with the Connecticut Pharmaceutical Association, and further VOTED to request Barnett Greenhouse, New Haven, to serve as Doctor Blanchard's replacement on the Committee for the remainder of the current year.

Request—Committee On Occupational Health

It was VOTED to authorize the attendance of J. Wister Meigs, Chairman, to attend the AMA Congress on Occupational Health (Houston, Texas; September 26-27-28) and to authorize payment of

ADVANCE NOTICE

COMMITTEE SERVICE QUESTIONNAIRE

Each year the Councilors from the eight constituent county medical associations assume the responsibility of selecting members of the Society to participate in the various programs of the Society which are carried on through the activities of committees and related groups. In making these selections, it is of importance to choose physicians who are not only willing and able to serve but also who are known to have an interest in the work of committees and groups to which they may be assigned.

In 1961, a "Committee Service Questionnaire" was mailed to all members as a supplement to Connecticut Medicine and from the returns this office was able to furnish the Councilors with a compilation of those who had a desire to be nominated for committee service. In order to update this compilation, a second mailing of the questionnaire will be made as a supplement to the November issue of the Journal. Members are urged to be on the lookout for the supplement, to indicate on it their areas of special interest, and to return the completed form to 160 St. Ronan Street, New Haven.

Dr. Meigs' usual expenses for such attendance (estimated at $300).

Report—Committee On Medical Economics And Insurance

Having been charged by the Council to review the complaint of a FCMA member against Group Insurers, Inc. (administrators of the Society-sponsored Overhead Expense Plan), the Committee reported its findings and recommendations as follows

Findings: The Committee finds that (the FCMA member) has no valid claim against Group Insurers, Inc. for overhead expense benefits, except that the latter's delay in notifying (the member) that his claim would be contested caused him to incur unnecessary expense in keeping his office open. The Committee finds further that the underwriter's offer to pay (the member) $1,500 in recognition of its responsibility for such delay is fair and equitable.

Recommendations: The Committee recommended that (the member) and Group Insurers, Inc. be notified of these findings, and that Group Insurers, Inc. be requested (in the future) to notify a policyholder within one week after filing a claim if the claim is going to be contested or the payment of benefits otherwise delayed.

It was VOTED to approve these findings and recommendations of the Committee on Medical Economics and Insurance, and to so notify the parties concerned.

The Committee also submitted several "incidental" findings and recommendations and it was VOTED to approve these as follows:

Findings: The Committee notes:

(1) That in nearly four years of continuous sponsorship by the Society, only one claim has been contested by an enrolled member.

(2) That three additional benefits have been provided to policyholders without any increase in premium; i.e., extension of the benefits period from 18 to 24 months; waiver of premium after six months of total disability; and a provision for partial disability payments following a period of total disability due to accident.

(3) That these evidences of member satisfaction and prudent fund management speak highly for the sponsoring relationship between the Society and Group Insurers, Inc.

Recommendation: The Committee recommends that Group Insurers, Inc. be asked to consider establishing some convenient method of periodically bringing to the attention of enrolled members that riders for medical conditions may, upon application, be removed at the discretion of the underwriters.

Request—Committee On Mental Health

It was VOTED to authorize the attendance of one member of the Committee at the AMA Second National Congress on Mental Health (Chicago, November 5) and to reimburse the member for usual expenses associated with his attendance (estimated at $225).

Site And Date—1964 Semi-Annual Meeting Of House Of Delegates

At the invitation of the Fairfield County Medical Association (extended by E. Tremain Bradley, Councilor) it was VOTED to hold the semi-annual meeting of the House of Delegates at the Stratfield Motor Hotel, Bridgeport, on December 9.

Site And Dates—1965 Annual Meeting Of The Society

The General Manager reported for Mrs. Lindquist and himself on their survey of the Griswold Hotel, Groton, as to its suitability as the site for the 1965 Annual Meeting. The survey was conducted as a consequence of a 1963 request of representatives of the New London County Medical Association that the Council consider holding the 1965 Scientific Session in that county area. The report noted that the premises of the Griswold are entirely adequate to accommodate the meeting; that the "resort" atmosphere and adjacent premises would make it possible to expand the social aspects of the meeting, if the Council so desired; that the travel time to and from Groton would be substantially increased for a good many members (as compared to a more central location); and that the earliest date available would be the third or fourth week in May.

After considerable discussion, pro and con, it was VOTED to hold the 1965 Annual Meeting at the Statler Hilton Hotel, in Hartford, on April 27-28-29. Expressing thanks to NLCMA for its kind invitation, the Council decided against the Groton site on the basis that it is not sufficiently central in location and will not be available until too late in the Spring.

Date of Next Meeting

It was VOTED to request the Chairman to set the date for the next meeting either on Wednesday, October 21 or Wednesday, October 28.

III. Old, New And Special Business

Report—Meeting Of AMA Committee On Osteopathy And Medicine

As requested by the Council, Max Caplan, Meriden, filed a comprehensive report on his attendance at a meeting of the AMA Committee on Osteopathy and Medicine, San Francisco, June 21, 1964. It was VOTED to accept Dr. Caplan's report, with commendation, and to submit same to the Editor of *Connecticut Medicine* for publication as information for all members of the Society.

Representative—AMA National Voluntary Health Conference

Having previously been asked by the Council to represent the Society at this Conference, Henry Caplan, Meriden, confirmed his intention of attending, Chicago, September 17-18.

Representative—AMA Fourth National Congress On Voluntary Health Insurance And Prepayment Plans

It was VOTED to direct the Chairman to appoint one or more members of the Society to attend this Congress, and to make his selections from among members of the Third Party Payments Committee, the Ad Hoc Committee on Resolution No. 2, or others concerned with the subject matter of the meeting. It is understood that the member appointed will be reimbursed for usual expenses incurred by his attendance. Dr. Martin later appointed E. Tremain Bradley, Norwalk, to represent the Society. The Congress is to be held at Las Vegas, Nevada, on October 2-3.

Progress Report—Financing Care Of The Acutely Ill And Premature Newborn

It was VOTED to accept as information, and with thanks, a progress report filed jointly by Samuel D. Rowley, Hartford, and Albert L. Larson, Hartford, on the work of an Ad Hoc Committee which is studying the problems of financing medical and hospital care of the acutely ill and premature newborn infant. It was further VOTED to request Drs. Rowley and Larson to keep the Council informed as to the progress being made in this study at such times as they feel are indicated.

"Five-Year Plan For Chronic Illness And Health Of The Aging Activities, Connecticut"

A document, bearing the above title, was submitted to the Council for possible "endorsement" by Harold S. Barrett, M.D., Deputy Commissioner of Health, and Project Director for the 150-member study group which prepared the draft of the "Plan." After studying the conclusions and recommendations of the document, and scanning the content of its several sections, the Council VOTED *not* to endorse either the submitted report or the plan outlined therein. It was further VOTED to notify Dr. Barrett and a number of other key persons associated with the preparation of the report of the reasons for the Council's decision in this matter, and to request an invitation for the Society to send official representatives to a Fall Conference to be held on the "Plan."

Memorializing Resolutions

In a series of actions, the Council adopted three memorializing resolutions as follows:

(1) Whereas: Norman A. Welch, M.D., of Massachusetts, has given many years of faithful and dedicated service to the American Medical Association and its members, therefore be it

Resolved: That the Council of the Connecticut State Medical Society, in meeting assembled on September 10, 1964, note with sorrow the untimely death of Norman A. Welch, M.D., and convey a message of deep sympathy to his widow and the members of his family.

(2) Whereas: Thacher W. Worthen, M.D., Hartford, has been a member of the Society for almost fifty years, was held in high esteem by his colleagues, and made signal contributions to the betterment of his community, his profession, and the field of surgery, therefore be it

Resolved: That the Council of the Connecticut State Medical Society express to the widow of Thacher W. Worthen, M.D., the deep sense of loss it shares with her in the passing of an eminent physician and citizen.

(3) Whereas: William J. H. Fischer, M.D., Milford, has been a member of the Society for over fifty years, and has distinguished himself through service to his profession, his patients, and his community, therefore be it

Resolved: That the Council of the Connecticut State Medical Society note with sorrow the death of William J. H. Fischer, M.D., and convey a message of deep sympathy to his widow and the members of his family.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on September 10, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Hartford National is particularly aware of the banking needs of the medical profession. We pioneered in Group Retirement programs, including PERP . . . a Qualified Pension Plan for Connecticut Physicians and Employees which takes advantage of new tax situations. Our Trust Division specializes in many other areas, too, including those below. So when you're talking to one of our Trust Officers, you are talking to a

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PLACEMENT OPPORTUNITIES

Litchfield County—Pediatrician and orthopedist wanted in Winsted, Connecticut area. This area is served by a small hospital and provides excellent opportunities.

Occupational Physician for state employee's clinic, located in Hartford. 35 hour week, 3 weeks vacation, up to 120 days sick leave, paid insurance program, social security and liberal retirement. Requires at least two years' general practice. Starting salary $11,640 going to $12,380 at end of year, then advancing $540 annually to maximum of $15,080. Reply directly to B. Dearington, State Department of Health, State Office Building, Hartford, Connecticut.

PLACEMENT WANTED

G.P. and General Surgeon wishes to locate in Southern Connecticut with either solo or group practice.

OBSTETRICIAN—GYNECOLOGIST—Board-eligible, 30, 4 years training. Would like to locate in Southern Connecticut.

Physician, age 35, Board-eligible in Internal Medicine, seeks salaried assistantship with internist or family practitioner. Connecticut license.

UROLOGIST—Well trained in large mid-western medical center; Board-eligible; 30; family; military obligation completed; desires association or group practice in southwestern Connecticut; available July 1.

DERMATOLOGIST—31 years of age; residency and internship completed; licensed in Connecticut; wishes either salaried Assistantship or partnership part-time in Ocmatology.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN.

Letter To The Editor

To The Editor:

At my request our Service Director has sent to our Branches throughout the state a copy of your fine article, "The Dying Patient's Grief." When I read this in Connecticut Medicine, it struck me as a keenly true and humane observation that well people and families of those who are sick often do not realize.

I believe the reading of this article will make us all the more understanding in our care of those who are ill. Thank you for letting us make use of your article.

Warm personal regards,

Edwin R. Meiss
Executive Director,
American Cancer Society,
Connecticut Division, Inc.

New Haven, Conn.

AROUND THE STATE

New Haven County

The New Haven County Medical Association will hold its 181st Semi-Annual Meeting at the Waverly Inn, Cheshire, Thursday, October 22nd. Business Meeting: 2:30 P.M. Social Hour and Dinner: 7:00 P.M. Speaker: Mr. John M. Lupton, Weston, Connecticut; Executive Director, State Republican Campaign Committee. Subject: "Predicted Political Trends in 1965."

Tolland County

The Tolland County Medical Association will hold its 182nd Semi-Annual Meeting at the Olde Homestead Inn, Somers, Tuesday, October 20th, at 6:30 P.M. Dr. Paul N. Graffagnino of Hartford will speak on the subject, "Child Psychiatry and the Brain Damaged Child."

1964 SEMI-ANNUAL COUNTY ASSOCIATION MEETINGS

October 13—Litchfield County
October 15—Middlesex County
October 15—Windham County
October 20—Tolland County
October 22—New Haven County

1964 MEETINGS

November 4-6—New England Postgraduate Assembly, Boston, Massachusetts
November 29-December 2—American Medical Association Clinical Convention, Hotel Americana, Miami Beach, Florida

1965 MEETINGS

April 27-29—Connecticut State Medical Society Annual Meeting, to be held at Statler-Hilton, Hartford, Connecticut

OBITUARY

William J. H. Fischer, M.D.

1883 - 1964

Dr. William J. H. Fischer died on August 29, 1964 at the Milford Hospital, Milford, Connecticut after a prolonged illness. His age was 81. The son of the late Reverend and Mrs. William A. Fischer of Danbury, Dr. Fischer was born in that city in 1883 Graduating from Concordia College, Bronxville, New York, he became the youngest licensed pharmacist in the State of Connecticut in 1904. He was 17 years of age at the time. He maintained his pharmacist license throughout his life, and it was a source of great interest to him that he was one of the few physicians practicing who could fill his own prescriptions. He entered Yale Medical School and graduated in 1911. After his graduation he served his internship at the Hospital of St. Raphael.

During World War I Dr Fischer served as Chairman of the Board of Examiners for the Milford Draft Board, a role he was to play again in World War II. In 1918 he gave up his practice to enlist in the U S. Army and served as Lieutenant in the Medical Corp. He received the U. S. Congressional Citation for his war service.

Besides serving on the staff of the Milford Hospital, which he helped to found, Dr. Fischer was also a member of the courtesy staff of the Grace-New Haven Community Hospital, the Hospital of St. Raphael, Bridgeport Hospital and St. Vincent's Hospital, Bridgeport.

A past president of the New Haven County Medical Association, Dr. Fischer was also a member of the New England Pediatric Association, the Hezekiah Beardsley Pediatrics Society, the Connecticut State Medical Society, American Academy of General Practice, Milford Medical Society and the New Haven Medical Association. He served as a member of the Executive Committee of the Connecticut State Board of Medical Examiners; as a member of the Board of Directors; chief of staff and head of the department of pediatrics at the Milford Hospital. He also founded the Hospital's Baby Clinic.

Dr. Fischer dedicated more than fifty years of his life to the practice of medicine, was unstinting in his efforts to encourage young physicians, hospital improvements and create and maintain a high standard of medical practice in his community.

Dr. Fischer is survived by his widow, the former Emma Doll, of Milford; a son, Dr. William J. H. Fischer, of Providence, Rhode Island; three sisters, Mrs. Julia Doll, Miss Henrietta Fischer and Miss Marie Fischer, all of Bridgeport; three grandchildren and a nephew.

With the passing of Dr. Fischer, his family, the medical profession and the community have suffered the great loss of a devoted family physician and friend.

WALDO E. MARTIN, M.D.

In Memoriam

Alderman, Irving—New Haven; Columbia University School of Medicine, 1919. Dr. Alderman actively practiced medicine in New Haven for 43 years. He was a member of the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, the American and Connecticut Societies for Physical Medicine and Rehabilitation, and the Phi Lumbda Kappa Medical Fraternity. Dr. Alderman died August 26, at the age of 72.

Davis, J. E.—Hartford; Johns Hopkins University, 1919. Dr. Davis was a prominent nose and throat specialist in the Hartford area for 35 years. He was a consultant to the State of Connecticut Prison in Wethersfield and to the City of Hartford at McCook Hospital and the Hartford Dispensary. He was a visiting otolaryngologist at Hartford Hospital. Dr. Davis was a member of the American Academy of Ophthamology and Otolaryngology, the American Medical Association, the Connecticut State Medical Society, the Hartford County Medical Association, and the Hartford

Medical Society. Dr. Davis died August 11, at the age of 71.

Worthen, Thatcher W.—Hartford; Dartmouth Medical School, 1911 Dr. Worthen served in the Army Medical Corps until he came to Hartford in 1918, where he became a member of the Hartford Hospital's medical and surgical staff, and served as its president from 1948 to 1950. He was then made an honorary member of the medical staff. He was a consulting surgeon at the Institute of Living, Mt. Sinai Hospital, Hartford, and Bristol Hospital, Bristol. Dr. Worthen was a member of the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. As a member of the Hartford Medical Society, Dr. Worthen held the positions of past president, chairman of the Board of Directors and chairman of the Building Committee. He was a fellow of the American College of Surgeons, the American Board of Surgeons, and the New England Surgical Society. Dr. Worthen died September 9, at the age of 78.

Doctor's Office

Frank K. Abbot, M.D. announces the removal of his office from 163 Grove Street to the Waterbury Medical Building, 1389 West Main Street, Waterbury.

Michael P. Atkins, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 57 Union Street, Rockville.

Morton Bender, M.D., announces the opening of an office for the practice of internal medicine and gastroenterology at 385 Main Street, West Haven.

Meredith M. Dickinson, M.D., announces the removal of his office for the practice of surgery to 1389 West Main Street, Waterbury.

William J. Hostnik, M.D., announces the opening of an office for the practice of plastic and reconstructive surgery, head and neck and hand surgery at 342 Montauk Avenue, New London.

Peter J. McLoughlin, M.D., has joined Thomas P. Birney, M.D. as a partner in the practice of pediatrics at 1984 Park Avenue, Bridgeport.

Harry Sigel, M.D., announces the opening of an office for the practice of dermatology at 2044 Bridgeport Avenue, Milford.

Albert Weinstein, M.D., announces the opening of an office for the practice of ophthalmology at 340 Capitol Avenue, Bridgeport.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Structure And Metabolism of Coricosteroids. Proceedings of a Symposium held in Paris, July 5, 6, 1963 and Organized by the Faculte de Medecine, Laboratoire de Chimie Biologique, Edited by Jorge R. Pasqualini and Max F. Jayle, Academic Press, London and New York, 1964, 156 pp., Illustrated, $6.00.

X-ray Technology. Third edition, by Charles A. Jacobi, B.Sc., R.T. (A.R.R.T.) and Don Q. Paris, R.T. (A.R.R.T.), C. V. Mosby Co., St. Louis, Missouri, 1964, 408 pp., with 306 figures, $11.50.

Modern Developments In Audiology. Edited by James Jerger, Academic Press, New York and London, 1963, 432 pp. Illustrated. $12.00.

Symptomology And Therapy Of Toxicological Emergencies. By William B. Deichmann, Ph.D. and Horace Gerarde, Ph.D., Academic Press, Inc., New York and London, 1964. 551 pp. $18.00.

Give and Take, The Development of Tissue Transplantation. By Francis D. Moore, M.D., W. B. Saunders Co., 1964, Philadelphia and London, 182 pp. Illustrated. $5.50.

Massage, Principles and Techniques. By Gertrude Beard, R.N., R.P.T., Elizabeth C. Wood, A.M., M.S., R.P.T., W. B. Saunders Company, Philadelphia and London, 1964, 163 pp. Illustrated by Vicki Catalini. $6.00.

Diseases Of Metabolism, Detailed Methods of Diagnosis and Treatment. Fifth edition, Edited by Garfield G. Duncan, M.D., W. B. Saunders Company, Philadelphia and London, 1964. 1551 pp. Illustrated. $28.00.

Corneal Contact Lenses. Edited by Louis J. Girard, M.D. and Associates., C. V. Mosby Co., St. Louis 1964, 318 pp. Illustrated. $19.75.

Cardiac Arrest And Resuscitation, 2nd Edition. By Hugh E. Stephenson, Jr., M.D., The C. V. Mosby Co., St. Louis, 1964, 448 pp. Illustrated. $15.00.

Synopsis of Pathology, 6th Edition. By W. A. D. Anderson, M.A., M.D., F.A.C.P., F.C.A.P., The C. V. Mosby Co., St. Louis, 1964. 839 pp. 406 text illustrations, 4 color plates. $9.75.

Dynamic Pathology, Structural and Functional Mechanisms. By Maurice M. Black, M.D. and Bernard M. Wagner, M.D., The C. V. Mosby Co., St. Louis, 1964. 281 pp. Illustrated. $8.00.

WOMAN'S AUXILIARY

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Mrs. Charles M. Krinsky, New London

President-Elect
Mrs. William R. Richards, New Haven

First Vice-President
Mrs. James F. Jones, Danielson

Second Vice-President
Mrs. David O'Keefe, Hartford

Recording Secretary
Mrs. Harry Levine, Fairfield

Corresponding Secretary
Mrs. Hilliard Spitz, New London

Treasurer
Mrs. Stephen A. Hulme, West Hartford

Health Careers

Mrs. Charles M. Krinsky, president; Mrs. Saul Karpel, co-chairman of Health Careers, and Mrs. William R. Richards, president-elect of the Auxiliary attended two meetings on Health Careers held at the hospital of St. Raphael in New Haven during August.

These meetings were attended by representatives of a cross-section of health organizations in Connecticut interested in developing a state wide coordinated career guidance and information program under a central agency to be known as the Connecticut Health Careers Council.

Dr. Bernard F. Mann, Jr., chairman of the committee on Health Careers for the State Medical Society was the chairman for these meetings.

At present the meetings are planning the formation of a constitution and a set of by-laws for the Council.

Auxiliary Workshop

Tuesday, September 22, 1964 was "Workshop Day" for members of the State Auxiliary. This workshop was planned to outline the 1964-65 program of the Auxiliary for all County officers, chairmen, committee members and other interested Auxilians.

Mrs. Charles M. Krinsky, president of the Auxiliary presided.

Dr. William R. Richards, General Manager of the Connecticut State Medical Society addressed the group on "Legislation-Pending and Passed."

State Officers and Chairmen outlined their programs and discussion periods were allowed.

Notes

Mrs. Charles M. Krinsky and Mrs. Irving H. Krall represented the Connecticut Auxiliary at the Eastern Regional Workshop Conference of AMA-ERF held September 17 and 18 at the City Squire Motor Inn in New York City.

The October meeting of the Board of Directors has been changed from October 20 to October 27.

Reserve Monday November 16th for the semi-annual meeting of the Auxiliary to be held at the Hotel America in Hartford. Details will be given later.

Congratulations to New Haven County for increasing their scholarship grants to five this year.

WOMEN'S PHYSICIANS DINNER

November 4, 1964

The New England Branch of the American Medical Women's Association will hold a Dutch Treat dinner, for all woman physicians, on Wednesday, November 4, 1964 at 6:00 P.M., at the Statler-Hilton Hotel, Boston, Massachusetts. November fourth is the first day of the New England Post-Graduate Assembly.

Please send your reservations to Esther Silveus, M.D., 43 Bay State Road, Boston, Massachusetts 02115.

NEW BOOKS IN REVIEW

TOWARDS EARLIER DIAGNOSIS. Keith Hodgkin with foreword by Sir Robert Platt. E & S Livingstone Ltd., Edinburgh & London, 1963. Williams and Wilkins Co., Baltimore 2, Maryland. 459 pp. $6.50.

Reviewed by: LOUIS H. NAHUM

The author points out the two main difficulties he encountered during ten years of general practice in Britain. One was that during his training in a hospital he did not encounter the diseases a doctor finds in practice and so he had to learn his profession by trial and error. The second difficulty is the need to have an efficient working knowledge of the early features of a wide range of diseases. These are encountered in practice and may or may not end up in a hospital. There is therefore a wide gap between hospital and general practice. How to prepare the student for the altered emphasis and different clinical material is the purpose of this book. The reason he was able to bridge this gap so successfully was his passion for keeping accurate records on all his cases exactly as he was taught to do while in the hospital.

In Part I consisting of five chapters he takes up techniques of making an early diagnosis, clinical pointers and subjective reactions that influence it and a good chapter on anxiety and psychoneurosis. He says many wise things and deals with the important psychological side of illness and the patient's individual attitude towards disease.

Part II deals with a large number of conditions which are never seen in hospital practice at all and also deals with early stages of disease which may reach a hospital. He presents the clinical observations that are needed to recognize the early stages of disease. He gives us an insight into how a family doctor works, thinks, and struggles to adapt his hospital training to the needs of a busy general practice.

"The family doctor is privileged to see the innermost workings of a patient's mind." The doctor must be careful not to go beyond the problem about which he has been consulted. Then he offers practical points in building up a patient's confidence in his doctor.

Educators who know nothing about problems in general practice would do well to read this book. There is a great need for good general practice and there is a great need to recognize how good it really can be. This book will contribute to a better understanding of the true function of the personal doctor.

PEDIATRIC THERAPY. Harry C. Shirkey, Editor. The C. V. Mosby Co., St. Louis, 1964. 72 Contributors, 1144 pp., 343 figures, 51 tables. $16.50.

Reviewed by: LOUIS H. NAHUM

What makes a good textbook is the editor and the contributors he has chosen. In the case of this excellent textbook, both have been happily combined. The editor is an extraordinary person who began as a clerk in a drug store, rose to be a pharmacist, finally an M.D. specializing in pediatrics. He practiced not long but intensively, had opportunities to see very ill children both at home and in the hospital, finally becoming a professor of pediatrics and an important person in the revision of the pharmacopoeia and the National Formulary. He was also a director in the Jefferson County Poison control center and perhaps this is why a most outstanding section of this book is devoted to poisons and their antidotes although the authors are James M. and Alan K. Dory, not the editor.

Not only are the qualifications of the editor very high but he has succeeded in assembling 72 outstanding contributors of national fame for the 96 chapters. All are extremely competent in the various sub specialized fields of pediatrics. Throughout the book, however, can be seen the hand of the editor in the common plan for all the sections and his personal hand in many parts of each of the 19 sections. It is a plan which lends itself to easy reading, concise statements of principles of therapy, and how they are specifically carried out. There is not one obscure or ambiguous procedure offered. This I suppose is because each author accepts full responsibility for his own plan although there are a few references at the end of each chapter to noteworthy ideas. The individual presentation of techniques clearly reflects the interest and personal experience of the authors as related to children and is clearly written for the treatment of infants and children's diseases.

The chapter on disorders resulting from poisoning and antidotes are particularly outstanding and will probably be an important reason for the extensive sale of this excellent book to students, interns, and pediatricians and physicians generally.

There is a considerable number of children that are hospitalized for surgical conditions. The student, house officers and practicing physicians have close contact with and responsibility for the care of such patients and it is especially worthy to have a part of the book devoted to surgical conditions and their management.

The last section is devoted to drugs, their purposes and their reactions and this itself will be rewarding to anyone possessing this book. In general the philosophy behind the book is first that pediatric therapy is important enough to stand on its own feet rather than as a part of general therapy. Second that our experience with drugs, both positive and negative makes it starkly evident that treatment is extremely important and should rank on a par with diagnosis. A good diagnosis is only the beginning. It must also lead to good therapy.

With this book diagnosis is mostly assumed and therapy takes the stage. It is thus that Professor Welch in his foreword emphasizes the real place of this book, it is for those who have a deep interest in treatment of disease. For such readers there will be great pleasure and satisfaction.

A final word must be said about the excellent format and printing. Large and small caps clarify the concepts, and double column on each page makes reading less fatiguing. Mosby has done its usual excellent publishing job.

STRUCTURE AND METABOLISM OF CORTICOSTEROIDS. Edited by J. R. Pasqualini and M. F. Jayle. Academic Press, London and New York, 1964. 168 pp., illustrated. $6.00.

Reviewed by: PHILIP K. BONDY

This book presents the papers delivered at a symposium of the Faculty of Medicine in Paris in July, 1963, and is concerned with the chemical structure of corticosteroids. It is divided into three parts. The first thirty pages are concerned with physical and chemical methods of studying corticosteroid function. The second, approximately seventy pages, is concerned with studies of the metabolism of various corticosteroids, particularly the intermediary metabolism in plasma and urine. Finally, the third part, representing approximately thirty pages, discusses the metabolism of the steroids in pathological situations — particularly Cushing's syndrome and renal insufficiency. The papers are all highly technical and demand a degree of chemical sophistication beyond the grasp of most practitioners. Although the data are well presented, many of the papers are preliminary and represent studies of only a small number of experiments and cases. This book will be stimulating and instructive to workers in this field, but at the present stage of development of endocrinology it does not provide anything of importance to the practitioner, even though he may have great interest in clinical endocrinology.

RADIATION AND IMMUNE MECHANISMS by W. H. Taliaferro, L. G. Taliaferro, B. N. Jaroslow. Academic Press, Inc., New York and London, 1964. 152 pp. $3.45.

Reviewed by: CARL F. VON ESSEN

This is one of the most delightful monographs that I have perused in the field of radiation biology and related topics. It is well conceived, well designed, and well documented. The authors present a lucid discussion of the fundamentals of immune mechanisms followed by considerations of radiation injury. From these two basic subjects they embark upon a detailed discussion based predominantly on their own work on the effect of radiation upon antibody responses following bacterial antigenic challenge. The ramifications of antigen dosage, timing, and radiation dosage and timing are explored. These interrelationships have application well outside the limited area of radiobiology and immunology since they encroach upon the newer fields of organ transplantation, autoimmune diseases, and the long-term effects of radiation upon the human population. Radiomimetic substances are now in use in the field of homograft surgery and a chapter on the action of these substances on antibody formation is included. There are 320 references presented in alphabetical order in addition to a large author index and a fairly complete subject index. This small volume is recommended reading to those physicians interested in the biology of ionizing radiation, in homograft surgery, and the hazards to the human population of ionizing radiation.

TEXTBOOK OF OTOLARYNGOLOGY, 2nd Edition by David D. DeWeese and William H. Saunders. The C. V. Mosley Company, St. Louis, Missouri, 1964. 523 pp. $9.25.

Reviewed by: BENJAMIN ALLEN

This is a well organized and well written book. It covers the broad field of otolaryngology—not in the extensive detail that the specialist might seek in the investigation of some special problem or in search of a fine surgical technique—but rather in a concise and practical way. This is as it should be. It is a text book pointed to the student and general practitioner. It reads easily. The illustrations are good. The authors who are professors and heads of their departments, Dr. DeWeese at the University of Oregon Medical School and Dr. Saunders at the Ohio State University College of Medicine, display the sound understanding of this specialty that one would expect of men in their positions. The text includes well written chapters on the mouth, the pharynx including the tonsils and adenoids, the nasopharynx, the larynx, endoscopy including the trachea, bronchi and esophagus, the nose and paranasal sinuses, and the ear including the mastoid and labyrinth. The section on the ear is particularly up to date as the authors have assembled the newer knowledge of the physiology of hearing, modern audiometry and a discussion of the operations for the improvement of conduction hearing impairment. There are also included chapters on the facial nerve, the salivary glands, cysts and other tumors of the head and neck, and a particularly well written and detailed chapter on speech disorders.

The one reservation this reviewer has is that greater detail and emphasis had not been devoted to bacteriology and allergy in otolaryngology, with particular reference to the indications for and the proper use of the antibacterials, the antihistamines and the corticosteroids. While it is true that these subjects are discussed at length in standard texts in bacteriology, allergy and therapeutics, nevertheless in this reviewer's opinion knowledge of these matters is of so much use and value in the daily practice in Ears, Nose and Throat that it seems important that their comprehensive coverage be an essential part of the modern textbook in this specialty.

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A brochure giving full details about the three-day program has been mailed to all members of the Society.

The Assembly is sponsored by the Council of N. E. State Medical Societies.

Registration Fee — $15.00

HARTFORD HOSPITAL SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS

October 17, 1964 - January 2, 1965

October 17 — *Research Forum*—9:30 a.m.—12:00 noon.
Subject: "Wound Infection Forum."

October 22-24 — (3-Day Visiting Surgeon) — C. Barber Mueller, M.D., Prof. of Surgery, Syracuse
October 22 — Operating and Rounds with Resident Staff.
October 23 — Surgical Path. and Surgical X-Ray Conferences.
Oct. 24 — H.H. Amphitheater.
9:00 a.m.: Subject Pending.
11:00 a.m.: "Problems in the Jaundiced Surgical Patient.'
October 24: 10:00 a.m. Grand Rounds.

October 31 — Alexander B. Gutman, M.D., Director, Dept. of Medicine, Mt. Sinai Hospital, N.Y.C.
Subject: "Gout."

November 7 — Edward Pulaski, M.D., Director, Div. of Basic Surg. Research, Walter Reed Army Instit. of Research, Washington, D.C.
Subject: "Present Status of Selection of Antibiotics."

November 14 — (Diabetes Week) — Searle Rees, M.D., Director, Baker Laboratories, Joslin Clinic, Boston, Mass.
Subject: "Current Concepts of the Pathogenesis and Treatment of Diabetic Microangiopathy."

November 21 — Howard Taylor, M.D., Professor of Obstetrics and Gynecology, Columbia P & S.
Subjects: 10:00 a.m.: "The Fibroid Puzzle."
11:00 a.m.: "Control of Cervical Carcinomas."

November 28 — Sevenson Flanigan, M.D., Assoc. Professor of Neurosurgery, Yale.
Subject: "Acute Management of Head Injuries."

December 5 — Robert S. Schwartz, M.D., Assoc. Prof. of Medicine, Tufts.
Subject: "Present Status of Serum Gamma Globulins."

December 10-12 — (3-Day Visiting Surgeon) — John M. Beal, M.D., Professor and Chairman, Department of Surgery, Northwestern.
December 10 — Operating and Rounds with Resident Staff.
December 11 — Surgical Pathology and Surgical X-Ray Conferences.
December 12 — H.H. Amphitheater.
9:00 a.m.: Subject Pending.
11:00 a.m.: "The Choice of Surgery for Peptic Ulcer."
December 12 — 10:00 a.m.: Grand Rounds.

December 19 — No Clinic.
December 26 — No Clinic.
January 2, 1965 — No Clinic.

GASTROENTEROLOGICAL CONVENTION

October 19, 20, 21, 1964

The 29th Annual Convention of the American College of Gastroenterology will be held at The Roosevelt in New York City, on October 19, 20, 21, 1964.

In addition to the several individual papers to be presented, there will be Panel Discussions on Gastric Freezing and on Benign Diseases of the Esophagus; Symposia on Gastrointestinal Hemorrhage; Gastric Mucosa; an afternoon of Round Tables on various subjects, and Motion Pictures. There will again be scientific as well as commercial exhibits and the sessions will be open to all physicians without charge.

On October 22, 23, 24, immediately following the Convention, the Annual Course in Postgraduate Gastroenterology will again be given. The moderators will be Dr. I. Snapper, Director of Medical Education, Brookdale Hospital Center, Brooklyn, N.Y., and Dr. John L. Madden, Clinical Professor of Surgery, New York Medical College; Director of Surgery, St. Clare's Hospital, New York, N.Y. The session will be held at The Roosevelt and at the Mt. Sinai Hospital. Attendance at the Course will be limited to those who have registered in advance.

Silver Certificates are to be presented to those who have been affiliated with the organization for 25 years.

The Annual Convocation Ceremony will be held at The Roosevelt on Sunday evening, October 18, 1964, at which time the principal speaker will be Dr. John L. Madden, who will receive an Honorary Fellowship from the College.

Copies of the program and further information may be obtained by writing to: American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.

FIRST NATIONAL CONGRESS ON STROKES

October 29-31

Palmer House, Chicago

The First National Congress on Strokes, designed to stimulate a wide-spectrum program of prevention and management of strokes and rehabilitation of stroke patients, has been scheduled for October 29-31 at the Palmer House in Chicago.

Sponsoring agencies are the American Medical Association, American Heart Association, Heart Disease Control Program of the U.S. Public Health Service, and Vocational Rehabilitation Administration of the Department of Health, Education and Welfare.

In announcing the Congress, Chairman Frank H. Krusen, M.D., of Temple University School of Medicine, Philadelphia, pointed out that the once hopeless connotation of the word "stroke" can be modified by newly developed concepts and techniques in prevention, and by practices developed in the last two decades in rehabilitation.

The high prevalence of strokes, third leading cause of death in the United States, is amendable to attack, Dr. Krusen said. But to be effective, all members of the community of health services must be willing to participate.

Physicians, nurses, therapists of all disciplines, administrators, social workers, psychologists, vocational counselors, community planners and legislators, all have great responsibility in translating the vision of new attitudes and practices into action on a large scale, he added.

In a message to local medical societies, Norman A. Welch, M.D., president of the American Medical Association, said that the program, which will be conducted by an outstanding faculty, will constitute an intensive course on pre-stroke detection, preventive medical and surgical techniques, medical care of the acute stroke patient and continuing care. He added:

"Because of the importance of stroke prevention, management and rehabilitation to the medical profession and to the people of this country, I want to urge each county medical society to have at least one of its members attend the Stroke Congress."

Following the opening session Thursday, the epidemiology, diagnosis and prevention of strokes will be discussed by Champ Lyons, M.D., The University of Alabama Medical Center; Jeremiah Stamler, M.D., Chicago Board of Health; Irvine H. Page, M.D., Cleveland, Ohio; Clark H. Millikan, M.D., Mayo Clinic, Rochester, Minnesota; Robert N. Baker, M.D., Veterans Administration Center, Los Angeles, and Michael E. DeBakey, M.D., Baylor University College of Medicine, Houston.

Panel sessions on the care of the early stroke patient will be held Thursday afternoon and Morris Fishbein, M.D., will speak at the Congress banquet that night.

Friday's session will include a discussion on convalescent and continuing care of the stroke patient by David Frost, M.D., Vocational Rehabilitation Administration, Washington, D.C.; Edward E. Gordon, M.D., Michael Reese Hospital, Chicago; David Gelfand, M.D., Philadelphia; Frederick J. Kottke, M.D., University of Minnesota Medical School, and Donald R. Sparkman, M.D., Division of Vocational Rehabilitation, Olympia, Washington.

Television demonstrations and "fireside" panels will also be held Friday.

Saturday morning's session will be devoted to "Community Programs for Stroke." Speakers will include Mathew Lee, M.D., New York University Medical Center; J. Gordon Barrow, M.D., Georgia Department of Public Health; John A. Lichty, M.D., Colorado Department of Public Health, Sylvia R. Peabody, Visiting Nurse Association; and Louis deBoer, Chicago Heart Association.

NATIONAL SPORTS CONFERENCE

November 29, 1964

The Sixth National Conference on the Medical Aspects of Sports will be held Sunday, November 29, in conjunction with the AMA Clinical Convention.

Many well known sports figures will speak at the daylong conference, sponsored by the AMA Committee on the Medical Aspects of Sports.

C. B. (Bud) Wilkinson, Oklahoma City, Okla., former University of Oklahoma football coach and athletic director, and consultant to the President's Council on Physical Fitness, will be a principal evening speaker. His subject will be, "Building Values Through Athletics."

James E. Counsilman, Ph.D., Bloomington, Ind., U.S. Olympic Swimming Coach, will give his "Reflections on the 1964 Olympics" at a luncheon session.

Tenley Albright, M.D., Boston, former Olympic Skating star, will participate in a discussion of "Sports for Girls."

Other speakers include Warren R. Guild, M.D., Boston, who will speak on "The Meaning of Endurance," and Robert A. Moore, M.D., Ypsilanti, Mich., whose topic is "Mental Health Through Sports."

Also on the program will be a symposium on "The Shoulder in Sports" and discussion sections on "Sports for the Teen-ager," "Environmental Considerations," and "Aquatic Sports.'

Thomas B. Quigley, M.D., Boston, Chairman of the AMA Committee and Harvard University team physician, will preside at the conference which will be held at the Deauville Hotel.

ST. FRANCIS HOSPITAL PEDIATRIC SYMPOSIUM

November 18 and 19, 1964

The St. Francis Hospital Pediatric Symposium will be held in the Amphitheater of the hospital in Hartford on Wednesday, November 18th and Thursday, November 19th. It is sponsored by the Department of Pediatrics and supported by the St. Francis Hospital Association. The program is as follows:

Wednesday, November 18th

10:00 a.m. Charles D. Cook, M.D. of Yale University *"Respiratory Problems in the Newborn."*

2:00 p.m. Fred S. Rosen, M.D. of Harvard University *"Immunological Deficiencies."*

Thursday, November 19th

10:00 a.m. Charles F. Barlow, M.D. of Children's Medical Center *"Neurological Diseases in Infancy and Childhood."*

2:00 p.m. Robert H. Parrott, M.D. of Children's Hospital of D.C. *"Recent Advances in Virology."*

Miami Beach Plays Host To AMA Clinical Convention

November 29-December 2

A scientific program attuned to the current needs and interests of the practicing physician is planned for the 18th clinical convention of the American Medical Association.

Immunization, depression, cardiac arrhythmias, vascular occlusive diseases, emphysema, iatrogenic diseases, and hypertension are only a few of the major areas to be explored during the four-day meeting, November 29-December 2.

More than 300 physicians will participate in a full program of lectures, exhibits, motion pictures, color television, fireside conferences and breakfast roundtables.

A new feature of the clinical convention this year is a postgraduate course on obstetrics for the general practitioner. Fifteen lectures will be presented during three sessions ranging from infertility and prenatal care through complications of labor and anesthesia to postnatal care and maternal mortality. Chairman of the course is Ralph W. Jack, M.D., Miami.

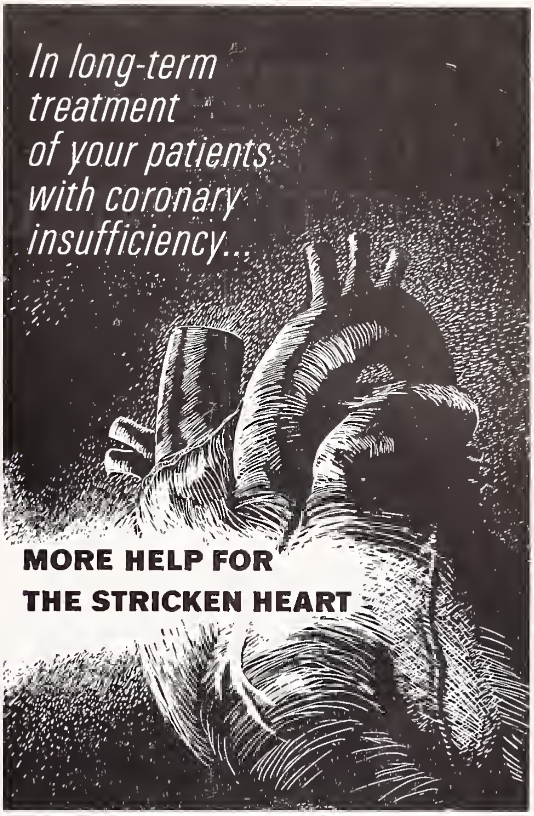
The entire scientific program, with the exception of the fireside conferences and breakfast roundtables, will be held in Miami Beach Convention Hall. The modern, single-level structure, completed in 1959, is fully air-conditioned and boasts one of the finest sound amplification systems to be found anywhere in the nation. It is located just one block from the Lincoln Road shopping centers, Florida's Gold Coast and the ocean.

The popular fireside conferences, presented as a joint session of the American College of Chest Physicians and the AMA, will be held Sunday night, November 29, at the Fontainebleu Hotel. There will be 11 tables at which 50 to 60 discussion leaders will engage in an informal and free exchange of views on a variety of medical subjects.

Six breakfast roundtables are scheduled at the di Lido Hotel. Topics include cancer of the thyroid, cosmetic surgery and peptic ulcer.

In addition, 125 scientific exhibits will be on display during the meeting, including a special exhibit on fractures, and some 30 medical motion pictures will be shown in the afternoon Monday through Wednesday.

General chairmen of the local committee on arrangements are Clifford C. Snyder, M.D., and Nelson Zivitz, M.D.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MEDICAL NEWS

Cytology And Pelvic Examination

On October 16 and 17, 1962 a demonstration program aimed at interesting adult women in early detection of pelvic cancer was held at the Norwalk Hospital. The program was sponsored by the Norwalk Branch, Connecticut Division, American Cancer Society. Members of the Attending and House Staff performed pelvic examinations and took cervical specimens for cytologic examination. With adequate assistance by volunteer clerks and Registered Nurses, and using several examining rooms per physician, it was found that each physician could readily perform 15 to 20 examinations per hour including the taking of a very brief regional history.

Although every effort was made to limit the patients to women who had never had a previous cytologic test it was eventually learned that 60 of the 256 were "repeats" and were already on file in our Cytology Patient Register.

Inasmuch as positive Cytologic tests decrease from about 1 in 200 on first examination of women over 35 to 1 in 1000 or less on subsequent examinations of those previously negative one may say that each of the 60 "repeats" decreased the chances of our detecting cancer by this technique.

The results of the survey are as follows:

Cytologic Examination

Class I or II	238
Class II, please repeat*	5
Class III or IV	0
Unsatisfactory**	13
	256

* Of these 3 were followed up, 2 were not. One of the 3 was then reported as Class III, had a cone biopsy, reported as chronic cervicitis.

** Of these 11 were repeated, all were I or II; 2 were not repeated.

Physical Examination

No abnormalities		209
Some abnormality (see below)		47
Fibroid tumors of uterus	9)	
Cervicitis	18)	
Cystocele		9
Cervical polyp		6
Ovarian cyst		2
Leukoplakia of Vulva		1
Inclusion cyst of Vagina		1
Urethral caruncle		1

Discussion

Although most of the 47 physical abnormalities detected were not life-threatening some of them either produced symptoms or were capable of producing symptoms. It is certainly more urgent to prevent agonizing and needless deaths from cervical cancer than to allay the chronic vaginal discharge of cervicitis or the discomfort of fibroids. However when patient days of disability prevented are used as a measuring rod, treatment of these "minor" ailments may also be very rewarding. In addition such potentially dangerous disorders as vulval leukoplakia and ovarian cysts were found.

Summary

Of 256 adult women subjected to pelvic examination and cytologic smears in a mass screening project, 5 were found to have somewhat atypical smears, none to have cancer. 47 had pelvic physical abnormalities felt to be of sufficient importance to warrant referral to a physician for treatment. It was concluded that pelvic examination is a practical and useful part of mass screening of adult women for pelvic disease. Cytologic examination is also a vital part of the program. The two methods of examination are complementary and together give the best care to the patient.

Roy N. Barnett, M.D.
Murat Merdinoglu, M.D.

1964—An Epidemic Year For Rubella (German Measles)

The latest figures released by the National Disease and Therapeutic Index (N. D. T. I.), which is a nationwide survey of private medical practice, shows visits for German measles reached epidemic proportions in the first six months of 1964. N. D. T. I., which measures the number of patient-physician contacts involving various diagnoses, estimated physicians received over 1.8 million visits for rubella (German measles) since January of this year. This represents almost a 500% increase over the same period last year.

Historically, the first half of the year accounts for the largest share of rubella visits. This can be clearly seen in the following table which shows a breakdown of visits for the years 1960 through June, 1964.

U.S. Patient Visits for Rubella (German Measles) by Calendar Quarter (000)

	1960	*1961*	*1962*	*1963*	*1964*
Jan.-Mar.	65	155	145	105	645
Apr.-June	215	220	215	220	1210
Jul.-Sept.	135	80	75	165	
Oct.-Dec.	80	65	100	100	
Annual Total	495	520	535	590	1855 (to date)

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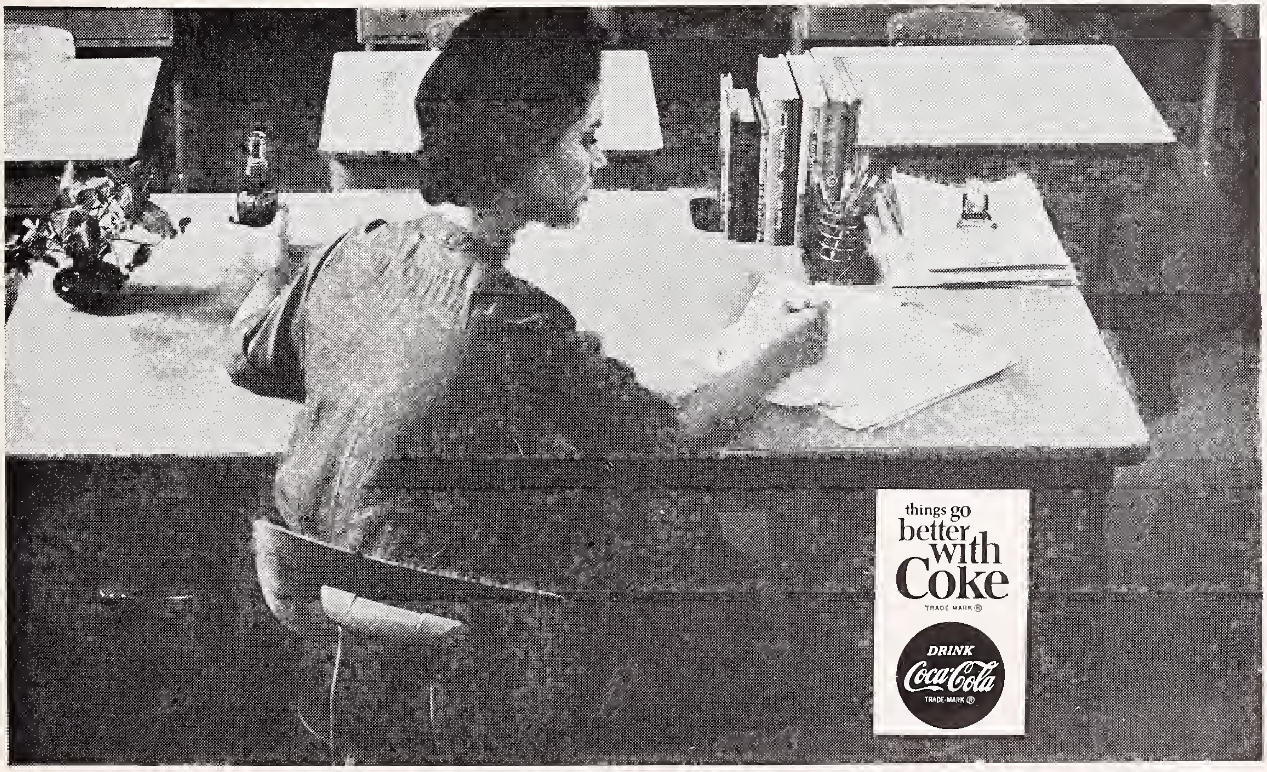


Whether you're a teacher correcting exams. A student cramming for them. A housewife cleaning up after the kids. Or a businessman working late at night. Whoever you are, things go better when you pause and refresh with ice-cold Coca-Cola.

A regional break of N. D. T. I. information shows that 1964 rubella visits were higher than average in the East, particularly in the New England and Middle Atlantic states. The Eastern half of the country usually accounts for 25% of all visits to private practitioners; rubella visits showed 36% in this region.

Regional Visits for Rubella (German Measles)

		All Visits to Private Phys.
	Jan.-June 1964	*July '63—June 64*
East	36%	25%
Mid-West	20	29
South	28	28
West	16	18
	100%	100%

N. D. T. I. further reported that an age breakdown on German measle visits showed that the epidemic was confined almost entirely to children and teen-agers with only about 1/5 of the visits being accounted for by adults. The sex breakdown for rubella was about average with females accounting for approximately 60% of the visits to private physicians.

Age of Patients with Rubella

			All Visits to Private Practitioners	
Age	*Jan-June 1964*		*July '63—June '64*	
0 — 9	61%	82%	15%	25%
10 — 19	21		10	
20 — 39	12		24	
40 & Over	6		51	
	100%		100%	

A.M.A. Clinical Convention November 29-December 2

In the American Medical Association's long history of fostering the continuing education of practicing physicians, the 18th clinical convention next November 29—December 2 in Miami Beach marks another milestone.

An excellent scientific program has been planned for the meeting. Particularly noteworthy is the postgraduate course on obstetrics, consisting of a comprehensive series of lectures by outstanding teachers.

Other sessions are devoted to timely subjects of wide interest and will be followed by question-and-answer or discussion periods. The fireside conferences and breakfast roundtables will provide further time for informal discussion.

There is today an acute awareness of the need for continuing education throughout the medical profession. Much effort is currently being exerted to provide better educational opportunities for practicing physicians. Yet, learning obviously remains an individual matter which rests on the personal initiative of each physician.

I urge every physician who possibly can to take advantage of the educational opportunity represented by the clinical convention. — Norman A. Welch, M.D., President American Medical Association.

Find Seasonal Changes In Gland Activity

The cortex of the adrenal gland appears to be more active in cold weather than in other seasons, a Japanese investigator reports.

Gen-Ichi Watanabe, M.D., University of Niigata School of Medicine, Niigata, Japan, studied adrenal cortex activity among a small group of men and women in Niigata City where quite severe hot weather immediately follows long cool seasons.

It appears that the adrenal cortex is most active during winter and is also active in hot weather but functions less in the mild seasons of spring and fall, Dr. Watanabe concluded from his study reported in the current Archives of Environmental Health, published by the American Medical Association.

It seems that either cold or hot climates may be stressful for man, he commented, and it is reasonable to assume seasonal physiologic changes although supporting evidence so far has been imperfect.

Due to the sudden temperature changes in Niigata City, he said, there is insufficient time for acclimatization. Under these circumstances, he said, climatic stresses, both hot and cold, may well activate the adrenal cortex.

The adrenal cortex secretes hormones which play a significant role in the body's defense against infections and other threats. Dr. Watanabe said his findings might help explain the varying incidence of certain diseases at different times of the year.

Activity of the adrenal cortex was determined in more than 10 men and 10 women by three tests performed at monthly intervals over a period of more than a year.

Hardening Of Cerebral Arteries Not Caused By Aging

Aging accompanies hardening of the cerebral arteries but is not a causal factor in this degenerative process, Drs. J. A. Resch and A. B. Baker, Minneapolis, said recently.

Their conclusion was drawn from a study of atherosclerosis within the circle of Willis based on 3,839 autopsies. A preliminary report on the study appears in the current Archives of Neurology, published by the American Medical Association.

Within the brain, true atherosclerotic changes are found chiefly along the vessels of the circle of Willis and the changes, even in the earliest stages, are visible to the naked eye, the authors explained.

The study revealed a correlation between age of the patient and atherosclerotic changes, where parts of the artery lining have thickened because of deposits of fat or other material.

"There can be no question that atherosclerosis gradually increases in the cerebral arteries with age," the physicians said. "This is particularly true of the more severe degenerative lesions.

"However, it is readily apparent that age alone is not specifically related to this process.

"In our series, the atherosclerotic process was first apparent in the second decade of life where five per cent of the cases showed some vascular changes. Our youngest patient was 14 years of age. Moreover, four per cent of our patients in the ninth and tenth decades of life showed no grossly visible atherosclerotic changes.

"These observations would suggest that age alone is not specifically related to this process but rather that atherosclerosis is a chronic degenerative disease of blood vessels requiring years for its development and in which many factors no doubt play an etiologic role. It appears more commonly in older individuals where the causative factors have ample time to produce the changes.

"Age, therefore, would be an accompanying factor rather than an etiologic agent in this degenerative process."

The study also revealed sex differences in the occurrence of atherosclerosis.

Cerebral atherosclerosis is less common in younger women than in men of the same age groups, the researchers reported.

This was particularly true in women between 40 and 60 who had from 11 to 19 per cent less atherosclerosis than men of the same age. Beyond the age of 60, the two sexes showed very little difference.

"From our present studies, it would appear that there probably is a sex difference in cerebral atherosclerosis and that this degenerative process is represented in women in the younger age groups in whom estrogenic activity is active," the authors concluded.

When a larger series of autopsies have been completed, the question of sex differences and the possible importance of estrogens, the female sex hormone, in cerebral atherosclerosis may finally be settled, they added.

The authors are affiliated with the University of Minnesota Medical School.

Potential Screening Method Described For Lung Cancer

A potential screening test for lung cancer was described recently by two Baltimore researchers in a scientific journal of the American Medical Association.

It might be possible to discover some cancer cases earlier by means of a simple test of the skin's electrical resistance, a technique currently used to map denervated skin areas, according to James F. Fries, a senior medical student, and Curt P. Richter, Ph.D., professor emeritus of psychobiology, Johns Hopkins University.

Writing in the current *Archives of Internal Medicine,* they said thousands of routine skin resistance tests at Johns Hopkins over the last 20 years revealed "striking patterns" in a number of patients with chest tumors, particularly lung cancer.

Skin areas of relatively high and relatively low resistance can be mapped by means of the test, according to the report. Relatively high resistance indicates denervated areas and certain patterns of denervated areas are believed to result from an underlying cancer.

The technique consists of measuring and recording resistance of the skin to a minute direct current. The current is transmitted by electrodes attached to a machine that indicates the degree of resistance, called a dermometer.

The test is quick, inexpensive, and causes no discomfort, the researchers point out. A mapping for screening purposes may take only 10 minutes. The equipment is portable and can be operated by a single technician.

"We have found lung tumors to cause four main types of patterns which are quite specific . . . as well as other abnormal patterns which cannot at present be considered specific," the authors said.

Of 37 patients with previously proved lung cancer, satisfactory records were obtained on 33 and 21 of these showed one of the specific skin resistance patterns, they reported. None had a completely normal pattern.

In one of these patients, the researchers added, "the pattern was so clear-cut that we are certain that the diagnosis could have been made at least six months and more likely a full year earlier by use of the skin resistance method."

Another group of 35 patients with a variety of diagnosed and undiagnosed chest diseases was screened for lung cancer by the skin resistance method, but only 1 showed a pattern characteristic of lung cancer. No diagnosis of cancer has been made in this group. However, the researchers pointed out that over a longer follow-up period, some of the patterns might prove to be due to cancer.

"It appears that the best results may be obtained with tumors of the upper lobes and apices, locations which have proved troublesome with some other procedures," the authors concluded. "False positives appear to be infrequent with this method.

"Should it prove true that all, or nearly all, lung tumors show at least nonspecific abnormalities of skin resistance early in their course, use of the skin resistance method as a screening test would give a smaller number of patients for more elaborate evaluation by other methods as well as being diagnostic in patients showing definitive patterns.

"Obviously, the satisfactory evaluation of a new method requires a large-scale experimental design in which skin resistance studies would be ordered at the same time as bronchoscopy and cytology in every patient with suspected bronchogenic carcinoma, and the results tabulated with regard to immediate results and long-term follow-up.

"We believe . . . that the potential of the skin resistance method is great and that large-scale studies may prove it to have a definite place among the battery of procedures used in the detection and diagnosis of tumors of the lung."

The authors did not compare skin resistance with other methods of diagnosis. However, they said lung cancer, now the most common malignancy in man, on the average is not diagnosed for three months to a year after the onset of symptoms and improved methods of diagnosis are needed.

No Harm Reported Due To Smoke From Charcoal Broiling

No ill effects resulting from charcoal-broiled food have been reported in man, according to Dr. Philip L. White, Sc.D., secretary of the American Medical Association Council on Foods and Nutrition.

The smoke which arises when drippings hit live charcoal used in outdoor grills is primarily from incompletely combusted fat, Dr. White explained in the current Today's Health magazine, published by the AMA.

"It is called thermal decomposition because fats begin to break down at temperatures under those required for ignition," he said.

"The same thing happens when frying fat begins to smoke when overheated.

"It has been shown that fat, which is partially decomposed by heat, produces substances suspected of being hazardous. However, no incidences of harm traceable to food have been reported in man. For that matter, research with appropriate animals likewise has failed to demonstrate any hazard."

To assure a more pleasant atmosphere when barbecuing, Dr. White said it is well to avoid the possibility of fat combustion as much as possible.

"The National Live Stock and Meat Board recommends that meat be cooked by the heat from the coals, not by fire," he pointed out.

"Any fires should be quickly extinguished by water. Coals should be spaced so that no two touch and adequate room is provided for fot to drip without coming into contact with the coals. Ideally, a drip pan should be used."

Alcoholism

Alcoholism is a growing disease problem confronted frequently by families, communities and physicians.

As with many other diseases it can be treated, but not really cured. The alcoholic can learn to completely control his disease, but the affliction cannot be stamped out so that he can return to alcohol without adverse consequences.

While the treatment primarily involves merely not taking a drink, the course of the treatment is often long, harrowing and beset by relapses. As with so many diseases, early detection usually brings about better results.

Among the signs of the disease are increased consumption of alcohol, often combined with constant thinking about drinking and making it an important part of life.

The alcoholic usually drinks more than he intends, or gets drunk when he doesn't intend to, for he uses alcohol as a drug rather than a beverage. Despite obvious excesses, however, he usually denies that he drinks too much or offers alibis for his drinking.

Other symptoms include getting drunk alone, taking an "eye-opener" in the morning, digestive disturbance and loss of appetite, and missing time from work or duties because of drinking.

Alcohol, aside from its addictive qualities, also has a psychological effect that modifies thinking and reasoning. One drink can change the thinking of an alcoholic so that he feels he can tolerate another, and then another, and another.

Most alcoholics cannot break the cycle alone, for it means giving up the thing in life he wants most.

Help for the alcoholic can come from many sources—the physician, the clergy, governmental agencies such as the local health department and volunteer organizations like Alcoholics Anonymous.

In addition the family can help by listening to his problems and helping him to face them realistically; encouraging him to help himself, but without scolding or lecturing him. And, when he gives up drinking, keep up his morale, emphasize his good points, not his bad ones. After all, he's sick, not wicked.

Tetanus Treated Successfully In Pressure Chamber

The use of high pressure oxygen therapy to treat nine persons with tetanus, or lockjaw, was reported in the current Journal of the American Medical Association.

"We have developed sufficient confidence from the response of these patients to hyperbaric oxygen to use it almost exclusively, and to eliminate essentially all standard modalities of treatment," Drs. Luke R. Pascale, Richard J. Wallyn, Samuel Goldfein anl Stanley H. Gumbiner, Chicago Heights, Ill., reported.

The authors are affiliated with the Hyperbaric Institute and departments of medicine and cardiology, St. James Hospital, Chicago Heights, and the Department of Medicine, Loyola University, Chicago.

The first four patients were treated with high pressure oxygen plus the other standard procedures. The fifth patient, with a mild form of the disease, underwent the same procedures with the exception of tetanus antitoxin. The sixth patient was treated exclusively with hyperbaric oxygen.

The other three patients had severe tetanus which standard treatment had failed to arrest. They received intensive high pressure oxygen therapy with the addition of only a sedative and antibiotics for other infections.

Conventional therapy, in essence, relies on the use of tetanus antitoxin, large doses of penicillin, muscle relaxing drugs, tranquilizers, and different forms of anesthesia, the authors explained. Despite these measures, they said, the mortality rate is 30 to 50 per cent.

It was believed on the basis of earlier research that the technique, which increases oxygen pressure 20 times the normal level, might detoxify the tetanus toxin, the physicians pointed out. Tetanus is caused by a toxin produced by the bacterium, Clostridium tetani, which infects wounds lacking oxygen. Oxygen inhibits the bacterium from generating the toxin.

Oxygen therapy was performed in a cylindrical decompression chamber, 18 feet long and 6 feet in diameter.

The major concern during therapy is that the patient may receive too much oxygen, according to the report. To avoid oxygen toxicity, therapy was interrupted at 15 to 20-minute intervals.

Oxygen therapy seems to have a direct effect on the course of the disease, the physicians concluded.

Cold Probe Used To Destroy Pituitary Tissue In 19

A freezing technique has been used for the surgical destruction of pituitary tissue in 19 patients suffering various disorders, it was reported recently in the current Journal of the American Medical Association.

Use of the cold probe was described by Drs. Robert W. Rand, Alfred M. Dashe, Donald E. Paglia, Louis W. Conway and David H. Solomon, Los Angeles.

A small vacuum-type tube, cooled to a temperature of from −170 to −184 degrees Centigrade by a liquid-nitrogen system, is inserted through the side of the head into the desired region of the pituitary gland, the authors explained. The temperature is reduced slowly to the minimum level and maintained for 10 to 15 minutes. During the procedure, the function of nerves which might be affected are tested every few seconds.

A surgical technique which can be performed with a minimum of risk is needed to treat patients with conditions requiring destruction of all or part of the pituitary gland, according to the physicians. Currently employed techniques have certain drawbacks and complications, they said.

Serious complications were not encountered with the cold probe technique in their series, the physicians reported.

Of the 19 patients, 13 had disseminated breast cancer. The response of these patients, "seems at this early date to be comparable to other modes of pituitary ablation, but accurate statistical evaluation must await a larger group of patients," the authors pointed out.

Of particular interest, they said, was the improvement following the procedure in one patient with acromegaly, a disease caused by overfunction of the pituitary which is characterized by enlargement of the bones and soft parts of the hands, feet and face. In six weeks, they said, there was marked reduction of the patient's headaches and swelling as well as striking improvement of her facial appearance.

No conclusions could be drawn concerning the results of the procedure in the remaining patients, four of whom had diabetic retinopathy, an eye condition which can be alleviated by pituitary destruction, and one with Cushing's disease, a syndrome resulting from overgrowth of certain pituitary cells.

The five physicians were affiliated with the departments of surgery, medicine and pathology, University of California, Los Angeles, School of Medicine, at the time of the study. Dr. Conway is now at Medical College of Virginia, Richmond.

Statistics Not Adequate For Comparing Health Of Nations

Vital statistics without careful interpretation have "little meaning" in comparing the health level among nations, the American Medical Association said recently.

In determining the health level between nations, factors other than the comparison of vital statistics must be taken into consideration, according to a report by the AMA Committee on Maternal and Child Care in the current AMA Journal.

"Comparisons based only on rates, ratios, or averages have little meaning unless differences in the demographic, social and economic structure of the nations being compared are noted," the committee said.

"Vital statistics must be viewed carefully to avert erroneous conclusions. Any comparative study must take into account differences between nations in view of the ethnic, economic, and geographical characteristics particular to each."

The committee pointed out general problems encountered in interpreting vital statistics and dwelled at length on infant mortality rates, an area where the United States has been compared unfavorably in recent lay and medical articles.

"Because of the many factors operative in the collection and use of statistics, errors of content can occur in the several stages of compilations and processing," the committee pointed out.

"In addition, errors of coverage include differences in the completeness of registration, in tabulation procedures, and in definitions of vital events.

"The reliability of vital statistics varies widely because no uniform legal specifications for the collection of data exist. In some countries, registration of vital events is compulsory for only part of the population. Other countries regularly exclude data for a segment of the population in which registration is not complete, though compulsory.

"The fragmentary nature of the resulting data is an important limitation in the use of vital statistics."

Complete vital statistics are judged to be those which represent at least 90 per cent of the total. Therefore, completeness may vary quantitatively up to 10 per cent.

In addition, the definitions of vital events are not uniform among nations. For example, there are differences in criteria for registering fetal deaths and live births. In most countries, "any sign of life" is the criterion for registration of live births, while in others it is more restrictive.

Because of this difference, the same event would be registered as a live birth and an infant death in one country but would be counted as a stillbirth or fetal death in another.

U.S. rates for general and maternal mortality and life expectancy compare favorably when rates for a combined population are calculated for nine European countries—the Netherlands, Sweden, Norway, Finland, Denmark, Switzerland, United Kingdom, Ireland, and West Germany.

The recalculated rates become 10.8 per 1,000 population for general mortality, 6.2 per 10,000 live births for maternal mortality, and 69.9 for average life expectancy at birth, while the U.S. rates are 9.5, 3.7, and 7.3 respectively.

"Calculating combined rates for the nine selected countries is like adding apples and turnips together," the committee commented.

"To compare a heterogeneous population with a homogeneous one, without reasonably accounting for the widely divergent origins, racial characteristics, and geographic, socioeconomic, and cultural differences, is equally questionable. The population of the 50 individual states of the United States differ as widely in these factors as do the populations of the nine selected countries."

The limitations of vital statistics "apply to an even greater degree to statistics on infant mortality," the report pointed out.

Perhaps the most important limitation is that in many countries a large proportion of the births are not registered until many years after occurrence. Relating infant deaths for any one year to births which occurred over a period of years produces a statistic of "little validity."

Since the mortality rate is based on the ratio of live births to infant deaths, any under registration of either factor will bias the rate.

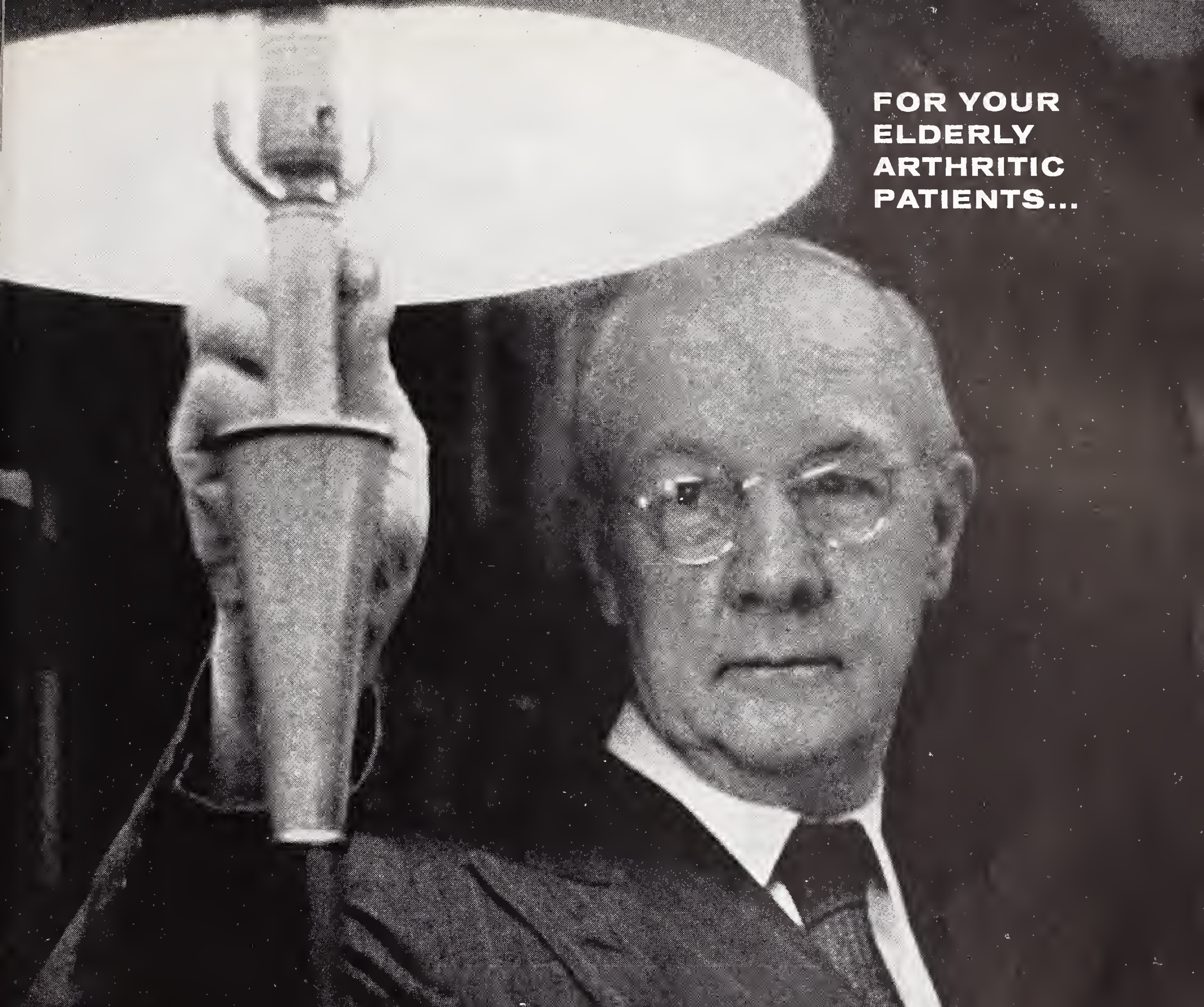
The committee cited variations in the practice of reporting data among the Netherlands, Sweden, Finland, United Kingdom and Ireland, concluding:

". . . differences in definitions and statistical practices in certain countries may result in an understatement in the infant mortality rate of from one to three percentage points compared with rates of other countries. There is an even greater uncertainty about measures of fetal loss, which also affect the infant mortality rate."

There are great variations in infant mortality rates throughout the world, the committee stressed. Rates differ according to income, occupation, social class, country, race, rural, urban and other factors.

With all of the variables to consider, the committee said, it becomes obvious that a smaller country such as Sweden, having a homogeneous ethnic, socio-economic structure, should not be directly compared with a vast heterogeneous nation such as the United States.

Comparing two relatively heterogeneous populations, such as the combined rate of the nine countries with the U.S. rate produces similar figures, 27



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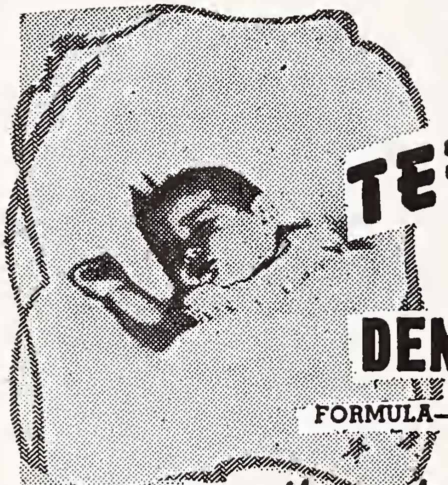

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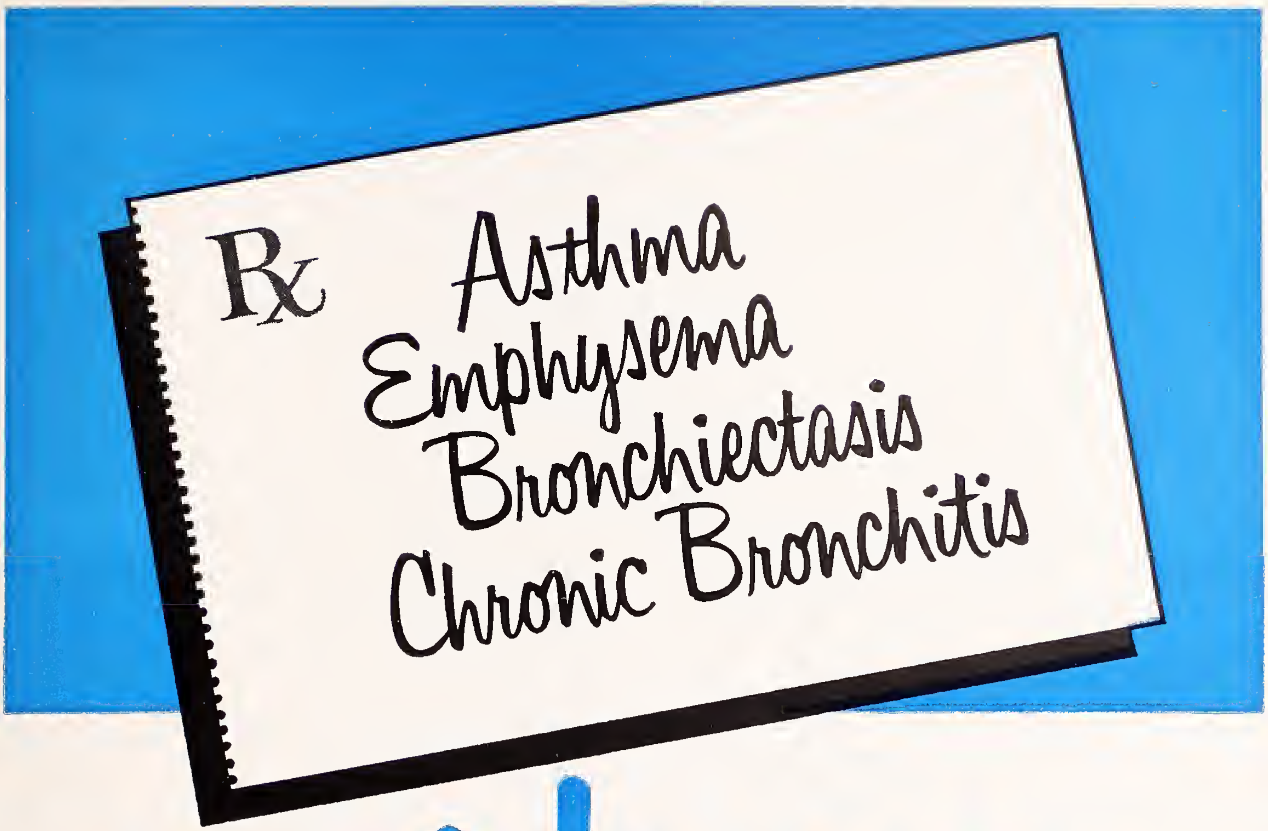

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infant deaths per 1,000 live births for the combined nations and 26 for the United States.

Similar rates also are found in comparing two homogeneous populatoins, such as a population within a small area of the United States and a similar homogeneous population in Europe.

"It is interesting to speculate about the reasons for differences found in infant mortality rates among populations but the real causes of these differences are unknown," the committee commented.

Since infant mortality rates are declining to low levels in many areas, the committee suggested that the next steps in research might be study of the relationships of infant deaths and sickness to maternal factors.

"Specific research on infant care practices, intelligence, and other personal factors of the mother is now essential," the report concluded. "This research could contribute toward further reducing infant mortality and morbidity."

Individual Air Conditioner Aids Man On Hot Job

An individual air conditioner providing cool, clean air for workers exposed to heat is being used routinely on certain jobs in industrial plants in the southern United States.

The simple, low-cost device is described by W. F. Lienhard, M.D., San Diego, Calif., J. P. Hughes, M.D., Oakland, Calif., and T. A. Brassette, M.E., New Orleans, in the current Archives of Environmental Health, published by the American Medical Association.

It could be particularly helpful for workers whose tolerance for heat has been reduced by aging, heart disease, or other physiological impairment.

Comparable observations on acclimatized workmen with and without the device during periods of identical work in a severely hot environment resulted in a threefold reduction in heat loss, a 25 per cent reduction in total heart beat, and a 50 per cent reduction in the rate of body temperature rise for the air-conditioned man, according to the researchers.

The entire weight of the personal air-conditioner is only 19 ounces, according to the report. The air is cooled by a vortex tube, invented in 1931 by a French metallurgist, George Ranque. Standard industrial compressed air is delivered through a hose to the tube attached by a belt to the man's waist. The tube converts compressed air at 120 degrees Fahrenheit to a steady flow at 65 F.

The tube develops a hot and a cold stream of air, the authors explained. The hot air is exhausted into the atmosphere while the cool air is supplied over the upper part of the body through perforated flexible plastic tubing worn beneath the worker's shirt. The cool air, which is of breathing quality, also may be dispersed through a semi-rigid funnel into a fabric hood and vest, both worn over the shirt. The air escapes easily through the clothing and from beneath the fabric hood.

Each worker has a "breakaway" coupling so he can detach himself from the air supply hose simply and quickly in case of danger. Hoses 150 feet in length provide the worker a high degree of mobility.

The vortex tube also has the potential application for body warming during work in extreme cold by adding an air mixing valve to vary the proportions of hot and cold air streams, the researchers added. In this way, output air between 65 and 80 F can be obtained when the temperature of imput air varies as widely as —20 F up to 130 F, they said.

None of the earlier systems proposed for individual air conditioning has been widely adopted in industry because in general they have been too complex and too costly for day-to-day use on most jobs, the researchers commented. Vortex tube units with accessory equipment are commercially available. The vortex tube alone costs less than $75.

Sharp Upturn In Stroke Deaths Found During Heat Waves

A striking increase in the number of deaths due to strokes has been found to coincide with heart waves, Michigan researchers reported in the current Journal of the American Medical Association.

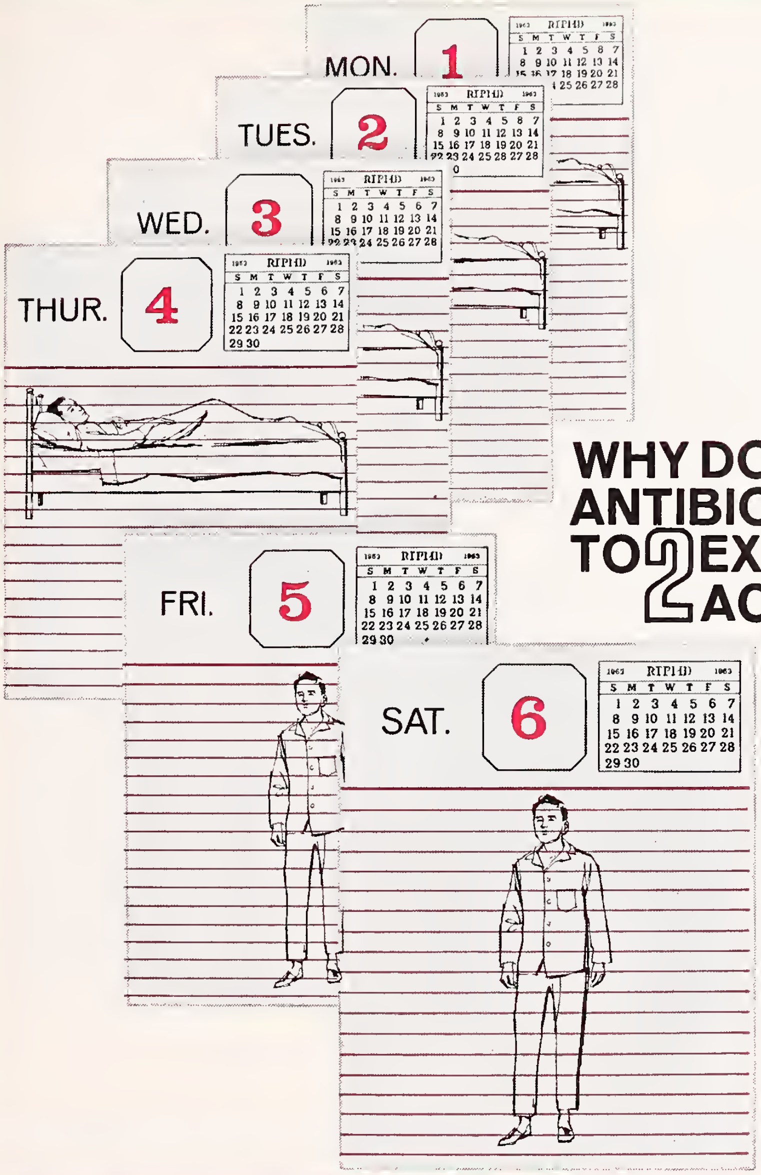
Deaths during heat waves occurring in Detroit in 1962 and 1963 were compared with deaths during other periods of the same years by Stanley H. Schuman, M.D., Ann Arbor, and Charles P. Anderson, M.D., and James T. Oliver, Detroit.

They found that the ratio of deaths due to cerebrovascular accidents (CVA) rose from an expected average of about 10 per cent of all deaths to an average of 15 per cent during the hot spells.

During the hot weeks of May 18, 1962, June 29, 1963, and July 6, 1963, 184 of a total of 1,212 deaths were attributed to CVA. During the weeks of June 30, 1962, July 7, 1962, and May 13, 1963, 98 of 994 deaths were attributed to CVA.

A similar rise in the CVA death ratio has been reported during the unusual late summer heat wave in Los Angeles in 1963, the authors pointed out.

On a national basis, more than 4,600 deaths above the computed prediction occurred in June



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and July of 1963, according to the report. These were recorded during heat waves in cities on the eastern seaboard and in Kansas City, Mo., Kansas City, Kan., Chicago and Detroit. Deaths in southern and western cities apparently remained at usual rates during this period. Persons aged 65 and older, representing less than 10 per cent of the general population, accounted for 38 per cent of the excess deaths.

An analysis of deaths in Detroit during the May, 1962, and July, 1963, heat waves showed a greater proportion of excess deaths occurred among the elderly, the Michigan researchers said. The Detroit cases also revealed that persons dying in heat waves were under medical care for a longer time than those dying in more temperate weather, and a larger proportion of heat-related deaths were among persons under medical care than among those in the comparison group.

The Michigan team also compared the average CVA death ratio for Detroit from May through August for 1962 and 1963 with the average for the city during the same months for 1953 and 1955. This revealed lower ratios for 1953 and 1955. Although July, 1955, was very hot with 18 days of 90-plus temperatures, the ratio was a normal 10 per cent and in August it was 1 per cent lower.

The reason, the authors commented, is not "entirely meteorological, but more probably concerns elements of medical diagnosis, therapy, and reporting which can strongly influence vital statistics."

The observed change in heat-related deaths between 1953-55 and 1962-63 may be associated with increased use since 1953 of diuretic drugs to promote the excretion of salt in patients with high blood pressure, they speculated. Total prescriptions for 1963 was estimated at 741,000,000, according to the report.

Drug-induced salt loss combined with the usual loss during heat stress may produce circulatory changes which predispose the elderly to strokes, they said, although such a relationship has not been proved.

Diuretics and other drugs to lower blood pressure undoubtedly have reduced the number of deaths due to cerebrovascular accident as complications of high blood pressure and heart disease caused by high blood pressure, the authors concluded. On the other hand, they said, sudden or prolonged periods of heat stress may require modification of such medication.

Drug Abusers May Number Far More Than Suspected

A survey at Boston City Hospital indicates that the number of drug addicts or abusers in the general population may far exceed previous estimates.

Results of an eight-month survey were reported by Drs. John A. Schremly and Philip Solomon in the current (Aug. 10) Journal of American Medical Association. Dr. Schremly is chief of Men's Addiction Service, U.S. Public Health Service Hospital, Lexington, Ky., and Dr. Solomon is physician-in-chief, Psychiatry Service, Boston City Hospital.

Those who took drugs, excluding alcohol, daily for one month when not medically indicated were considered drug abusers for purposes of the survey. All patients age 15 and over admitted to the hospital's emergency floor between October, 1961, and May, 1962, were screened by house officers. The authors made a further random check during four months of the study by interviewing every 20th patient admitted.

About 100,000 patients were admitted during the study period, and 82 drug abusers and addicts were discovered, according to the report. Forty-four were addicts, 32 to heroin, and 38 were abusers, 17 to barbiturates.

Of the 82 cases, house officers working alone detected 28. While house officers and the authors worked side by side, the house officers detected 41 cases and the authors, who were more experienced interviewers, detected an additional 13 cases by the random sampling.

The authors concluded:

"If the same ratio held and all patients admitted had been seen by us, presumably some 260 hidden cases might have been discovered! The implication is that there may be far more drug abusers and addicts in the general population than has ever been suspected (apparently three per thousand)."

Although drug abuse and addiction has been a social problem since the latter 19th century, there are no reliable incidence or prevalence statistics currently available, the two physicians pointed out.

"Increased interest and attention to the problem of drug abuse and addiction in new patients being admitted to a large general hospital may elicit many hidden cases otherwise undetected," they commented. "The failure of proper interest and attention may account for another order of magnitude in the underestimation of drug abuse and addiction in the community.

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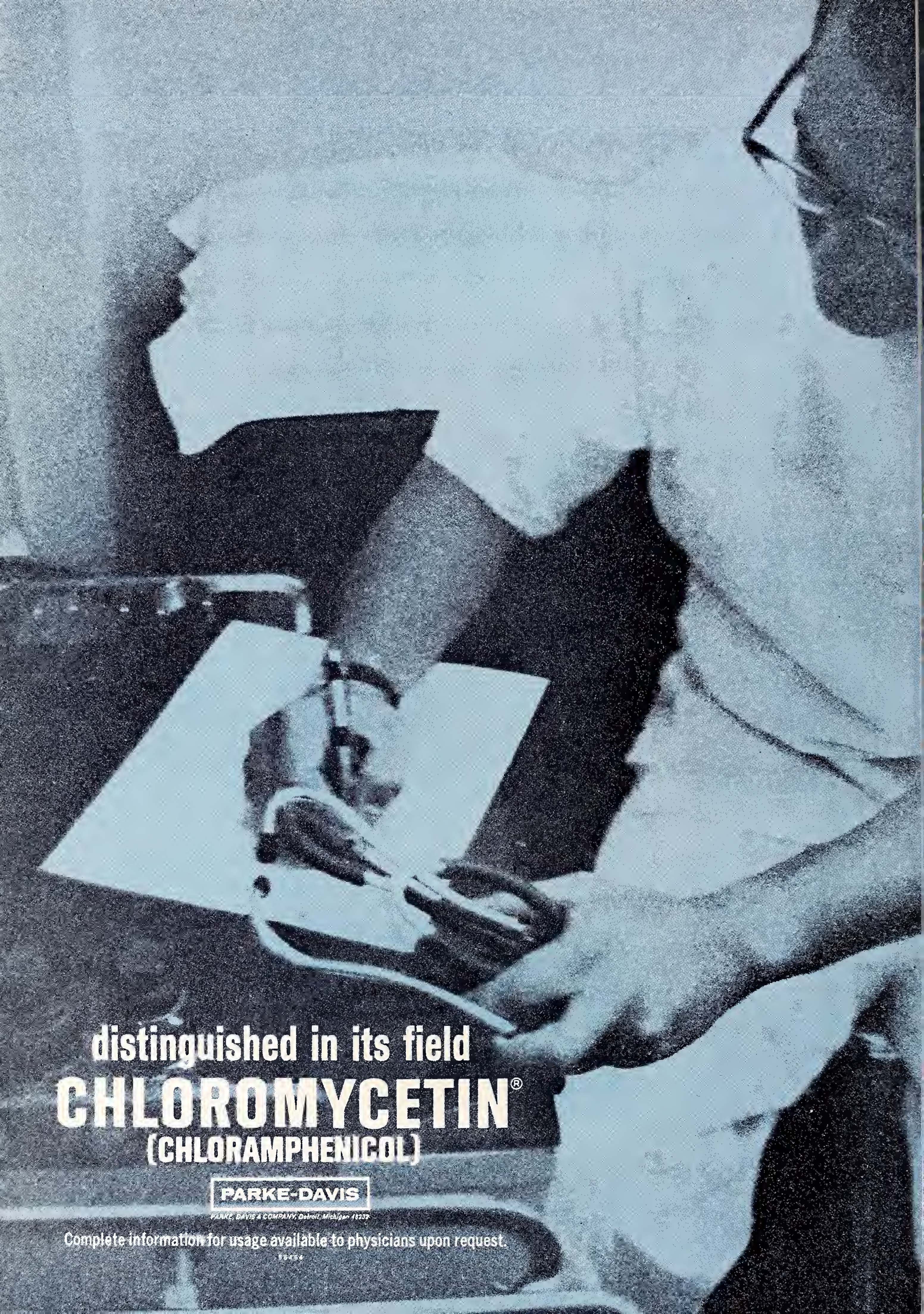

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Connecticut Medicine

editorials

Science Tools:

10. New Methods For Heart Studies: The Electrocardiorecorder

The electrocardiogram is a static affair in which the record is obtained by connecting a patient to the instrument. The patient is immobilized and the record is transient. But what would we learn if the subject had the greatest possible freedom of activity if we could obtain adequate samples over a twenty-four hours period eliminating the artificial and unrealistic situation of resting quietly on a comfortable pad with calm confidence in or fear of the physician.

The early attempts towards freedom, the elimination of entangling wires, required an individual to remain within range of radio receiving and electrocardiographic observing equipment, had the disadvantage of being subject to occasional radio interference. The next stage was the development of a portable radio receiver tape-recording unit to be carried by a subject free to go where he wished as long as he took the "ECG briefcase" and left it in his general environment. But still needed was further freedom from such baggage and from radio interference, plus a means of rapidly studying the long magnetic tapes obtained. The next development was the "electrocardiorecorder" which is free from connecting wires from the restrictions of staying in one locality, freedom from inconvenience of carrying electronic baggage and freedom to make recordings of any described length and still be able to analyze them. Now one can study the heart action of swimmers, forest fire fighters, broncho riders, etc.

The instrument is a small portable unit measuring 20 x 10 x 5 cm. and weighs a little over two pounds, can be carried in a man's coat pocket or woman's strap-type handbag, or is fastened to the chest during the period of observation. But a long record is only useful if it allows for locating rapidly, parts of interest, and so there is an analyzer which permits a ten hour record to be examined in ten minutes. A synchronized clock tells the observer the time of day for any part of the tape, so that changes can be correlated with activity. As a result, the so called arrhythmographic part of the analysis unit presents rapid quantitative compact information or pulse irregularities while another part of the so called AVSEP is used to observe changes of form.

The medical uses of this system are many. They include detection of subclinical angina, potentially serious arrhythmias, and some transient heart disorders such as paroxysmal atrial tachycardias, all of them not recognizable during orthodox electrocardiography which however will continue to have its uses in the measurement of established heart conditions. Then there are the real life situations in which heart studies can be made. Two of Holter's[1] subjects equipped with the units have been involved in automobile accidents. In each case both the unit and subject survived, but in one, the accident precipitated an attack of angina pectoris.

One can think of research uses for such a device also. What produces the recognized variability in pulse rates over an extended period the known variabilities from alcohol, nicotine, caffeine, fatigue, tension can be quantitatively measured. What if any significant electrocardiographic changes might occur during a normal active day in a clinically

THE COVER

CANNON: PHYSIOLOGIC INVESTIGATOR

WHILE a first year student at Harvard Medical School, Boston, in 1896, Walter Bradford Cannon (1871-1945) employed newly discovered X-rays to study activities of digestive organs in animals. Preferring cats, Cannon induced them to eat radiopaque meals, and followed food through alimentary organs with the aid of a fluoroscopic screen. Basic studies of digestion, and of effects of emotions on it, led to new understandings of food utilization, of transmission of nerve impulses, and of actions of endocrine glands. Second Professor of Physiology at Harvard, Dr. Cannon earned world-wide respect as a researcher, as a teacher, and as an ambassador of scientific good will.

normal person. What happens to the electrocardiogram with eating, exercise, sexual and other emotional activity, fatigue, sleep, etc. Not only can such a device be used to expand our knowledge of heart activity but someone will certainly turn to fashioning an electroencephalorecorder to free a brain test subject from his radio received environment.

Freedom through elimination of wires, restricted location, electronic baggage and radiointerference, gives us a glimpse of the future which is not too remote in which human beings and other animals will be wired for research. With numerous little boxes piling up information about body function we will learn much about physiological and pathological variables which now escape us for lack of recording, coding and analyzing systems.

L.H.N.

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Rapport: 1. Its Nature And Function

The growth of specialization in medicine has admittedly increased the expertness in the management of disease, but concomitantly it has diluted the rapport between the doctor and patient. It could very well be that those who sigh for the "good old days" are really missing a doctor- patient relationship which in itself can be a therapeutic mechanism. This is especially true of the patient suffering from nervous illness who may gain marked relief of symptoms by the simple process of forming rapport with the doctor. Some have believed that the therapeutic effect of forming a rapport is brought about by suggestion. But this can hardly be so. For instance, a dying patient who knows he is dying may still feel very much better by being visited by a doctor with whom he has rapport. We know that a short ten minute visit by an anesthetist to a patient the night before operation gives the patient a sense of security, calms his anxiety and reduces the need for pre-operative sedatives.[1] While it is true that emotional support and satisfaction of dependent needs are mediated through rapport, without doubt, the actual experience of this relationship itself has some therapeutic effect. What then is it? What is its function? How is it formed? What are the barriers to the formation of rapport and what are the common errors in its formation?

Several types of emotional relationships exist between doctor and patient. There is the bedside manner of the general practitioner, the rapport of the psychotherapist, the transference phenomenon in psychoanalysis and the hypnotic rapport of the hypnotherapist. In each of these a skillful physician can alter the quality of the relationship according to the special needs of the patient at any particular moment. The relationship is an important part of all medical practice and can be an important factor in restoring the patient to health.

The simple doctor-patient relationship is the basis of the bedside manner. In this the patient respects the doctor for his professional competence. It is this respect which facilitates the ordinary business of practice, and helps the patient cope with the psychological difficulties inherent in the doctor's history taking, and the patient exposing his body in the physical examination with the least possible upset. The physical examination may require the doctor to handle parts of the body the patient hardly touches, and the psychological examination often necessitates talking about things not ordinarily talked about. In the examining room the doctor-patient relationship has evolved in our culture so that this may be done without erotic involvement or psychological disquiet.

In the establishment of the simple doctor-patient relationship both doctor and patient know what to do. They each have their role. As soon as either one fails to accept it—if the patient involves the doctor in a social or political relationship or vice-versa then this changes the relationship. To save both patient and doctor from psychological disturbance it is necessary that each behave according to his appropriate role. The doctor in his manner, attitude and general behavior acts appropriately for a physician and brings a professional atmosphere with the proceedings. The success with which the doctor-patient relationship is formed is more closely dependent on the way the physician indirectly communicates his personal integrity than on his academic qualifications or technical skill as a doctor.

We must remember that rapport is the emotional adjustment between the doctor and his patient and that this makes psychotherapy possible. If the physician succeeds in communicating his personal integrity, then the rapport becomes something much deeper and more significant. The patient comes to trust the doctor, to have faith in him. Then he finds that he can talk with the doctor about his problems in a way he cannot with other people. He comes to feel his doctor understands him as an individual, not just his illness and his problems. He is led to feel that this doctor can help him.

The feeling that this doctor can help him is determined by emotional mechanisms and seems quite independent of any objective logical appraisal of the doctor's skill. In the simple professional relationship primarily skill and competence is involved. But if rapport is established another

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exclusive element is added. The patient feels that this is the doctor who can help him to the exclusion of all other doctors. For practical purposes the patient can have rapport with only one doctor at a time, and retains it no matter how many other specialists the doctor has resort to in consultation.

Rapport is never one sided. There is interaction. The doctor comes to respect the patient as an individual within the framework of their professional relationship. The doctor shares in the emotional relationship and it is important to realize this. It is based on the patient's feeling toward his doctor as a real person and the doctor's emotional reaction. The fact that the doctor himself is involved in the emotional relationship of rapport implies that he must ever be on guard to keep examining his relationship critically. At times he will need to modify it when necessary and so use it to greater advantage for the needs of the individual patient.

If the doctor understands his role and the patient his, if the doctor indirecelty communicates his personal integrity and exhibits his interest in the patient's problem, the foundation is laid for rapport which can become an important therapeutic mechanism.

The formation of rapport is not enough. We must strive to successfully control this relationship for it is of the utmost importance in the management of anxiety, an almost universal component of illness and often an illness by itself. We must think of rapport as a therapeutic mechanism in itself. It also makes it possible for other therapeutic mechanisms to function effectively. The physician who cultivates rapport will be in possession of a powerful tool often neglected by the specialist. His patient especially if suffering from a nervous illness may gain marked relief of symptoms by the simple process of forming a rapport with his doctor.

Rapport would appear to be an essential prerequisite for the effective use of almost all other therapeutic mechanisms especially the psychologic ones. We have seen[1] that simple explanation and reassurance are much more effective against a background of rapport. In psychoneurotics it is essential for suggestion. It makes conditioning easier and it helps with abreaction. It seems to be the basis of hypnotherapy. Without rapport the patient will be unable to ventilate the significant conflicts with which he is beset.[2]

Many a patient who comes to a physician is so to speak "on guard." Otherwise he could be open to attack upon his ego. To let himself go off guard he lays himself open with otherwise well guarded secrets exposed. The more anxious he is the more alert and guarded he will be. The more insecure he is the more difficult it will be to let go. This is where rapport comes as so important. Rapport achieved through unlimited trust in the physician gives the patient the necessary security and he can then let himself go off-guard. In short, trust is an important ingredient in the emotional relationship of rapport.

L.H.N.

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Suppression Of Glandular Activity: 2. Control Of Ovulation

When Djerassi in 1954[1] simplified the methods of steroid synthesis, this led to the clinical application of the newer progestins for control of ovulation and the management of dysfunctional bleeding and endometriosis. It can safely be said that this method to produce anovulation, ranks as one of the important contributions in gynecology. Flowers in a recent paper[2] has described the effects of ethynoylestradiol 3 methyl ether mestranol and nor-ethynodrel (Enovid E) in 259 patients through 3,510 menstrual cycles. The study was carefully controlled and the clinical evaluation included endometrial biopsy studies.

The combination of nor-ethynodrel and mestranol suppresses ovulation and causes regression of the endometrium. The mechanism of action is complex and not completely understood. They may act by suppressing follicle stimulating hormone and luteinizing hormone or by direct action on the ovary.[3] Flowers believes that pituitary gonadotrophins and endogenous ovarian hormones are both inhibited. Mestranol supports the endometrium and maintains uniform growth while norethynodrel causes sufficient secretory effect to prevent hyperplasia and at the same time sufficient suppression of the endometrium to make an unfavorable environment for nidation. Since estrogen and progesterone have separate but complementary functions, various combinations have been tried to obtain an agent which is economical, has few unfavorable side effects and is effective at the lowest possible dose.

The original norethynodrel-mestranol tablet (Enovid) Flowers points out, contained 9.85 mg. of norethynodrel and 9.15 mg. mestranol. A second tablet with half the dosage of each component was also found to be an excellent ovulation inhibitor and also caused satisfactory endometrial regression. The potency of norethynodrel as a progestin and the ability of mestranol to inhibit ovulation indicated that a logical combination to evaluate would be 2.5 mg. of the progestin and 0.1 mg. of the estrogen. It is this combination that Flowers investigated and reported upon.[2] The lower dosage of the drug proved completely reliable as an oral contraceptive. There were no medication or patient failures. It is significant that two of his patients who were pregnant at the time they began therapy, were not affected and completed their pregnancies successfully. This of course indicated that the dosage of the progestin was sufficiently low so that its regressive effect on the endometrium was easily neutralized by the pregnancy hormones.

It is known that a potent estrogen will generally cause nausea in ten to twenty per cent of patients until physiological adjustment occurs. This was also found in Flowers' series. About twenty per cent reported some nausea in the first ten days of the initial cycle. Only six per cent suffered some nausea during the twenty days of the initial cycle and only two per cent had to discontinue medication because of nausea and gastro-intestinal complaints. Some problems of intermenstrual bleeding and early menstruation and amenorrhea are well discussed by the author and management is developed based on recognition of the effect of the hormones on the pituitary gonadotrophins and endogeneous ovarian hormones. Essentially the major and important pharmacological effects of the progestins is to produce regression and progestational exhaustion of the endometrium. It is interesting that no thrombophlebitis was observed, no increase in the size of the uterus took place, and medical management proved so simple that it could be handled on the telephone by a well-trained office nurse!

The lower dosage of the drug, however, had other side effects which proved to be a dividend over and above the contraceptive effectiveness of the medication. Eighty per cent of the women reported a reduction in amount of discomfort of menstruation. Premenstrual tension was reduced in half. Fifteen per cent of patients suffering from profuse and prolonged menstrual periods resumed normal mentruation. Four patients who had endometrial hyperplasia developed regression of the endometrium and patients with endometriosis had reduction of pelvic pain even though the dosage of the constituents in the pill (Enovid E) was so low.

The reason of course that premenstrual tension was reduced, prolonged mentrual periods were corrected and endometriosis controlled, was because the oral progestin produced such fundamental changes in the endometrium. The contrast between the microscopic appearance of non-treated and treated patient's endometrium was striking and is explained by the pharmacologic differences of the effects of progesterone and the ninteen nor-steroids on the endometrium. Progesterone produces a well-developed secretory activity and increased vascularity and succulence of the endometrium which sets the stage for nidation. Norethynodrel on the other hand, causes progestational exhaustion of the endometrium and a reduction in vascularity that prevents nidation, reduces menstrual flow and discomfort and neutralizes hyperplasia. Thus the patient receiving the drug has progressive endomentrial regression rather than progressive secretory activity.

The question whether an oral contraceptive will adversely affect pituitary adrenal thyroid or ovarian function is important. Several studies already published[4,5,6] have thus far found no unfavorable effects. One could theorize that if one rests the ovary and the endometrium it might prolong in fact the reproduction years and delay the menopause. Indeed resting the ovary apparently improves fertility in some patients. Present data indicate that oral contraceptives used for as long as seven years and the suppression of gonadotrophin and ovary by the large doses of norethynodrel-mestranol required to treat endometriosis, has not interfered with the ability of the patient to conceive and bear normal children.[7]

Endometrial cancer is associated with excessive estrogen stimulation and hyperplasia of the endometrium. We have seen above that one of the major therapuetic effects of the oral progestins is to correct hyperplasia of the endometrium.[7,8,9] One would expect therefore that a reduction in endogeneous ovarian hormone and regression of the endometrium by the oral progestins would likely reduce the incidence of endometrial cancer rather than increase it. The drug used by Flowers did not change the chromatin pattern or the cytoplasmic nuclear ratio of cervical cells on the Papanicolaou smears. Others have reported similar results.[10] Although on theoretical grounds one would expect a reduction in the incidence of endometrial cancer as a result of the use of the oral contraceptive, the true incidence has not yet been determined since patients who have received these agents have not entered the decade, in which endometrial cancer is prevalent. However, a drug which removes the basis for cancer formation should not be feared as being carcinogenic. Furthermore, chronic cystic mastitis may also be avoided by the use of progestins and we are aware of the relation of chronic cystic mastitis and breast cancer from the detailed studies of Womack[11] on the endocrine relationship between chronic cystic mastitis and breast cancer.

It is clear that endocrine suppression can be used as a powerful tool in many gynecologic conditions with safety.

L.H.N.

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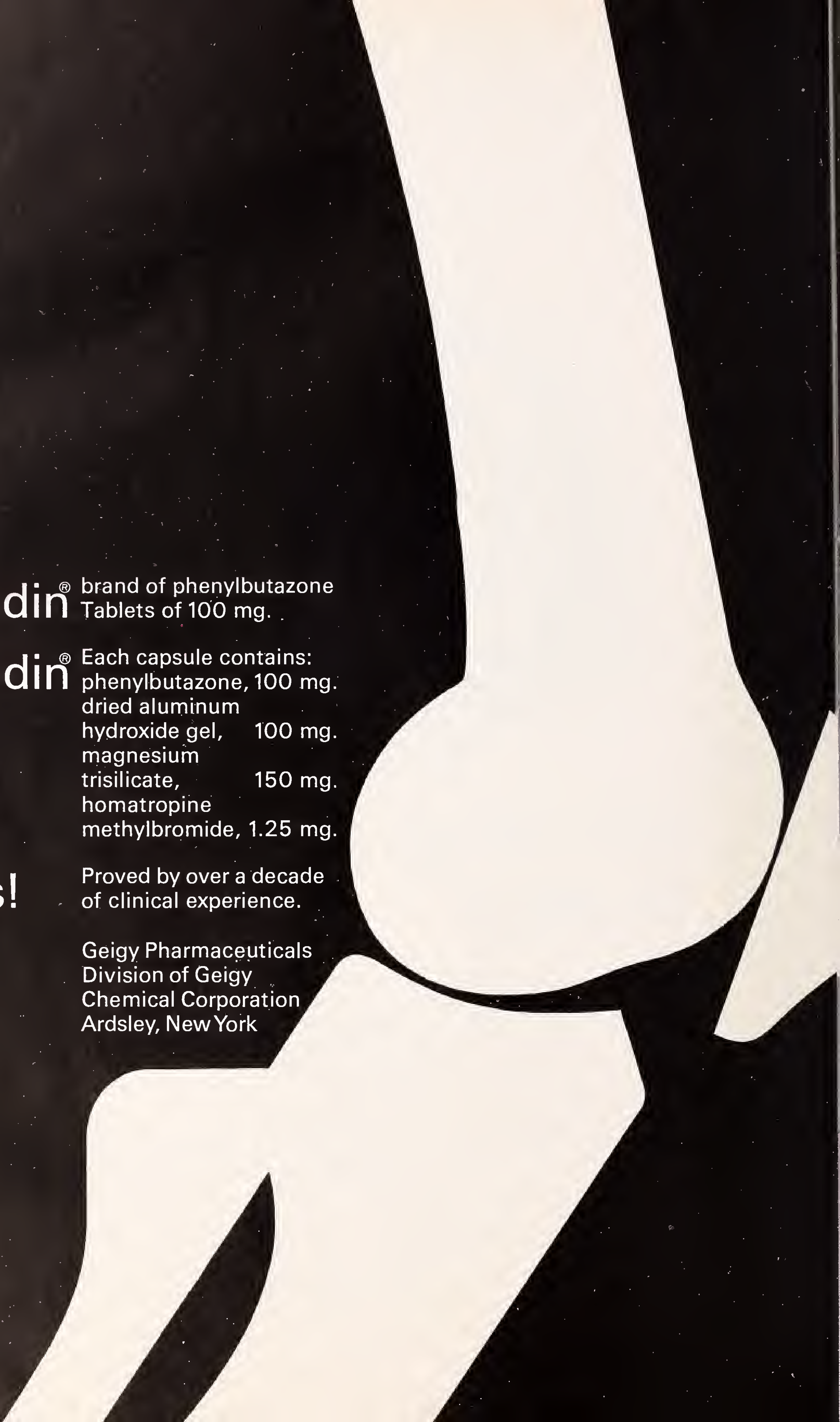

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Diagnostic And Therapeutic "Levels" In General Practice

The progress of medicine in the past one hundred years has depended on the recognition of the common diseases. Doctors have been trained to understand illness largely in terms of the natural sciences and many will regard their patients' emotions as a consequence of the illness and irrelevant to the current situation or as altogether extraneous to the task at hand. As a result, we may operate in terms of clichés; a "sick person is bound to be anxious or depressed;" "whatever the person's emotions, pneumonia is pneumonia and needs antibiotics;" "the doctors job is to relieve or cure the illness and not to become entangled in the patient's emotional troubles." Such an approach is too impersonal, makes out of medicine a listing of symptoms and signs both positive and negative and a choice of treatment that a computer or robot could do as well as the doctor. On such a level neither the doctor nor the patient need be human beings at all. Such an approach is bound to lead to misunderstandings, frictions, and disappointments; even worse, it may lead to misdiagnosis and wrong treatment, as a recent case report by Clyne[1] makes crystal clear.

Dr. Clyne visited Joan who was ill with fever, hoarseness, headache and sore throat. The treatment simple; expectorants, antipyretics; and the prognosis good. She could be expected to recover in a few days. This kind of case history is the daily bread of general practice and treatment based chiefly on anatomical and physiological considerations. It takes no account of the patient, young or old, happy or unhappy, rich or poor. The patient is devoid of most human attributes, she is "faceless." So was the doctor; his role one of impersonal objectivity.

But he soon discovered further symptoms. There was much emotional overlay. The patient was crying, two unwashed, unkept children were running about the room. Then Joan told a further story. Her husband, a corporal, was away on exercise. She could not cope with the children. Each time he was away she got sick. A certificate to the C.O. enabling her husband to come home always solved her problem. She was very dissatisfied with service life. Emotional elements such as her distress, obvious dependence on her husband, now came into the picture and the doctor was given a new role to bring her husband back. Dr. Clyne could now be either a sympathetic person and furnish a certificate but interfering with the soldier's duties, or gotten her some agency help which the patient obviously did not want. In either case, the prognosis would be similar, the acute illness would have improved in a few days and recur at the time of the husband's next exercise. Joan would have remained dissatisfied with service life and the unavoidable separation and the husband would have been in camp worrying about his sick wife and neglected children.

Joan has now changed from a faceless case to a human being, a young mother lonely, distressed and with social difficulties, somebody we can visualize, sympathize with, and understand. The doctor too had become human, he had felt with this patient in her human condition and to decide about the certificate in the light of his moral and social obligations. On this level, both patient and doctor had become involved with each other as human beings, Joan placing a responsibility on the doctor for a certificate for her husband's return. If the doctor accepts the role Joan assigned to him either by giving or refusing to give a certificate, he becomes a part of what in psychological parlance is called "acting-out." The patient's excessive dependence upon her husband and her urge to have him returned has been transferred from her "inner world" to the real world in the person of the doctor.

Emotionally disturbed people often act-out. If they do so in their own homes or at work they may hurt themselves or others. If in the doctor's presence and the doctor becomes a part of it, the patient's suffering may be unduly drawn out. Had Dr. Clyne accepted the role Joan assigned to him by giving or refusing to give a certificate, nothing would have changed psychologically or therapeutically. So he did neither, but let the patient talk on.

It developed that in telling her story she exhibited a great deal of aggression and hostility towards her husband who was distinctly older than she. She began to experience frigidity, dyspareunia and they had many rows about their unsatisfactory sex life. She nagged her husband to seek a discharge because his going away on exercises and similar duties caused her great anxiety. Then she revealed that whenever he went away she felt he might never come back. This kind of a story obviously stemmed from deep conflicts arising in childhood. With skillful guidance by Dr. Clyne, the story unfolded further. She was the youngest of five children, her father's pet. She spoke with much feeling about him who had held her on his lap kissing and fondling her, an exciting experience. But she had been a naughty and aggressive girl and especially disobediant to her lenient father. Then he had gone away and died. The patient took this very badly and for a long time was unable to get over her mourning.

Joan's condition became clear. It was one of sexual and dependent difficulties rooted in her deep attachment to her father. Evidently, in her older husband she had married the image of her father. Freudian doctrine explains that "the little girl within her" having been excited sexually by a loving father, felt the sexual stimulation as an incestuous, forbidden act and reacted against it with sexual inhibition and a feeling of guilt. She had been naughty and disobedient to her father and she was aggressive towards her husband during rows. Dr. Clyne reasoned that when one is angry with a person, one often feels, thinks or says, "I wish you were dead." It was now easy for Dr. Clyne to understand why "the little girl" having been angry with her father at home should feel guilty when he died suddenly (her terrible wish had come true!), and why the wife of the corporal should fear that a similar fate might befall her husband when he went away on exercise. The ill assorted mixture of love, hate, fear, and guilt within her, led to her depression and illness, but how pharyngotracheobronchitis could result from an inner conflict is not so clear.

Of course, the treatment of her real illness was to give the woman a chance to talk in a therapeutic catharsis about her emotional experiences to a neutral sympathetic listener. But this would not have been enough without the psychotherapeutic technique of interpretation, of making the patient aware of some of the interrelations of her feelings and actions and of the motivation of some of her wishes and actions. Joan had now become a complete human being with feelings, conflicts, suffering, truly alive, pitiable and understandable. By the end of the interview the question of a certificate had not come up again.

The doctor too has risen in status during the interview from a robot to a social worker and giver of certificates, and finally, to an expert in helping a sick person at the source of her morbid conflict. Now the doctor's work has attained a different quality and interest. In dealing with the throat infection, his tools were those of hospital medicine acquired as student and reader of text books on medicine. On such a level the case was utterly uninteresting: a feverish cold, the question of a certificate, pure triviality. Yet when the interview rose to psychobiology, the situation became humanly and scientifically interesting and important. Basic human emotions could be observed at work at the starting point of illness. Furthermore, for the doctor to make sense of the illness, he needed a type of training and equipment badly needed to make general practice into a rewarding specialty. For he could place the simple illness within the framework of a human being and her relation to others. He could discover now how the patient in her role as the "eternal little girl" had tried to make him wave his magic wand of certificate as if he were benevolent powerful father-like image. The doctor was able to see "what made the patient tick." It is a type of comprehension not often understood or used in the busy life of the average physician.

Our training and working habits in medical practice have led us to neglect the vast reaches full of interest and scientific possibilities to be discovered in general practice on the level that regards the patient as a whole person in her physical, social and emotional context. This cannot be achieved by a sympathetic attitude only . . . "poor woman, she is depressed because her husband is not here" or merely by intuition, kindness and ordinary every day human understanding.

Medicine of the type mentioned above, dealing with the whole person who is ill, requires specific skills and tecniques which can be learned by study and application. Many general practitioners learn them painfully by hit and miss methods in the course of practice but most made inadequately. Perhaps in the future, psychotherapeutic training will become a routine part of clinical training and will be recognized as the most important part of education for general practice. Skill in this field alone would be sufficient to set the general practitioner apart as a specialist and make his work most important and most rewarding.

L.H.N.

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The Thymus: 1. Its Role In Lymphocyte Production

No species could survive without a defense system capable of dealing with foreign invaders. In invertebrates, the only methods available for the destruction of pathogens are phagocytic and enzymatic mechanisms. Most vertebrates have these also, but in addition, they have developed an immunologic apparatus which enables them to produce specific reactions to limit the spread of pathogens and to prevent damage immediately in subsequent attacks. This system functions by the production of specific antibodies or immunoglobulins, the development of delayed hypersensitivity (such as tuberculous sensitivity) and the rejection of grafts of tissue from foreign donors.

From phylogenetic studies we learn that the evolution of such an immunologic appartus depends upon the appearance of the thymus and organized lymphoid structures. From ontogenesis we have learned that the period at which lymphoid elements especially the lymphocytes can first be identified is the time when immunity begins to appear. The thymus gland is the first organ in which lymphocytes can be clearly recognized and its lymphocytes are known to arise by direct transformation of the epithelial cells from which a part of the thymus originates.[1]

If the lymphocytes in the thymus arise by direct transformation of the epithelial cells, how do the lymphocytes in other regions arise? Theoretically, of course, they could originate independently of thymus lymphocytes and in a similar way. The appendix may be such a source as also the bursa of Fabricius. However, according to morphologic studies the lymphocytes appear first in the thymus and only later in the circulation, spleen, lymph nodes, alimentary tract and other tissues. In fact in some species they appear as late as the time of birth. They are numerous in the thymus where they show mitotic activity. They are scarce elsewhere until after birth, and outside the thymus, show practically no mitotic activity before birth. These observations have given rise to the hypothesis that at least some lymphoid elements arise primarily in the thymus. Subsequently they migrate, at various times before or after birth depending upon the species, to sites where they establish centers for the further development of lymphoid structures. If this were so then the development of immunologic responsiveness should depend on the establishment of a functioning lymphoid system whose cells, those that are concerned with immunologic reactivity, are derived from the thymus. It is obvious that experiments of various types are necessary to test the validity of this conclusion.

If the thymus is the main if not the sole organ producing lymphocytes what happens after birth. We know much about this problem from rodents. In these animals throughout life the rate of multiplication of lymphoid elements in the thymus is about seven times higher than that of lymphoid cells elsewhere. Even with advancing age with an involuted thymus, its production of lymphocytes takes place with almost the same intensity as in the young thymus and it is always greater in the thymus than it is in lymph nodes. Furthermore the rate of production of lymphocytes in the thymus is not affected by autogenic stimulation nor by resection of other lymphoid organs, nor by partial resection of the thymus itself nor by implantation of thymus grafts in the same animal. Nevertheless thymus lymphocytes do respond to the same general hormonal influences which affect lymphocytes throughout the body.[1] Such observations lead one to suspect that the strong stimulus for the proliferation of thymus lymphoid cells must arise within the thymus itself and must depend on certain structures widely dispersed in the thymus. In fact there has been described a special association between specialized reticulum cells widely distributed throughout the thymus cortex with mitotic lymphocytes.[2]

It has often been assumed that one of the main activities of the lymph nodes is lymphocyte production. However, no such production is found in germ free animals. Their lymph nodes are atrophic, their follicles are poorly formed, and the cells show no mitotic activity. The thymus, however, in such animals is well developed and actively lymphopoietic. This experiment implies, that if an animal's lymph nodes are unstimulated by challenging antigens, the follicular centers remain inactive and the cortical lymphocytic fields are devoid of mitotic activity and immature lymphoid cells or blasts are absent.

We know that one of the effects of antigenic stimulation is to increase the total cell population in the lymph nodes and spleen. Then follicular centers, "secondary nodules or germinal centers" appear and become actively lymphopoietic. A plasma cellular reaction is induced later. Stated another way, mitotic activity of lymphocytes in lymph nodes apparently occur only after antigenic stimulation.

The foregoing observations suggest that proliferation of lymphocytes is primarily a function of the thymus and that active lymphocyte production in lymph nodes and presumably in the spleen occurs only as a result of antigenic stimulation. They suggest further that the cells which proliferate in the thymus even in the absence of antigenic stimulation, are the precursors of some of the lymphocytes which appear in the lymphoid tissues and in the circulation. On the other hand the cells proliferating in the secondary nodules of the lypmh nodes and spleen can be thought of as the precursors of cells which respond to a booster injection of antigen and which play some special role in the secondary response.

If the hypothesis is to be held that the thymus is a primary source of lymphocytes, then clearly some sort of lymphoid cell must come out of the thymus. It is easy to study this problem by labelled cells. With such a technique it is possible to follow lymphocyte migration. This has been done in the guinea pig, a species in which significant lymphocytic migration from the thymus takes place well before birth. In this animal there are surprisingly small numbers of labelled cells seeded out of the organ. The simplest hypothesis would then be that the thymus is an important source of circulating lymphocytes. The lymph nodes on the other hand would provide a meeting place for circulating lymphocytes and antigen brought there by afferent lymph. It thus would become a site for the subsequent proliferation of those cells that have interacted with antigen.

Under normal conditions after birth, the circulating pool of lymphocytes have a long life span and therefore the thymus would have little to contribute. However, in the antigenically stimulated animal, the secondary lymph nodes in the spleen and other nodes may contribute to the circulation, lymphoid cells capable of mediating secondary immune response. We know that under such circumstances depletion of lymphocytes occurs rapidly. In such a case the thymus might be required again to build up the pool of circulating lymphocytes by a direct cellular contribution. We need here to postulate that some built-in mechanism probably of a hormonal nature exists to stimulate the thymus to cell proliferation, to safeguard the animal against depletion of lymphocytes such as occurs under conditions of stress.

L.H.N.

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Implications Of Renal Artery Stenosis

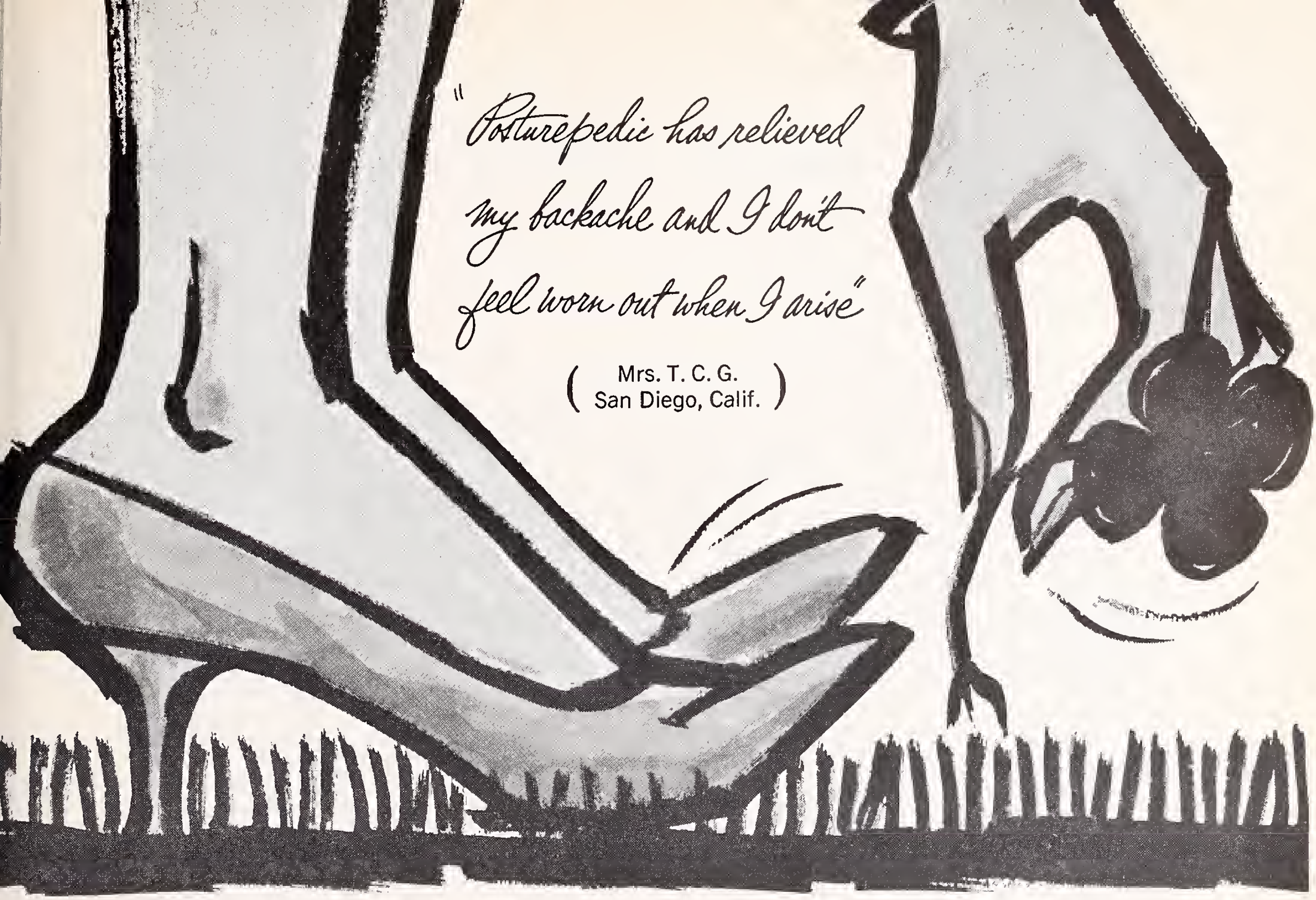
Hypertension can be a ravaging disease leading to untold complications, prolonged invalidism, and premature death. It is not surprising therefore that its mastery has led to intensive investigations along two major paths; drugs that can lower the arterial pressure to safer levels, and methods to search for the curable types. Among the latter are recognition and removal of pheochromocytoma elimination of progressive chronic pyelonephritis and revascularization of stenotic renal arteries.

Advances in vascular surgery have made possible re-establishment of blood flow distal to stenotic lesions of the renal arteries with many reported instances of permanent relief of hypertension. This has made it mandatory to determine whether renal artery lesions are indeed present in our hypertensive patients. Arteriography does permit excellent visualization of the renal vascular anatomy. However, what to do once a stenosing lesion of the renal artery is found? Of course, it is known that when hypertension is of relatively recent origin and the patient shows a unilateral renal artery stenosis associated with evidence of diminished function on this side, then amelioration or even complete relief can be obtained by surgical revascularization of the involved kidney or even nephrectomy.

However, the relationship of bilateral atheromatous renal artery stenosis to hypertension is not as precise as is the case in unilateral lesions. Especially in patients over forty years of age we find stenosis of renal origin as a result of atheromatous lesions which are commonly bilateral and in such patients the predictability of obtaining relief of hypertension by surgical means is less well established. In many cases of bilateral atheromatous renal artery stenosis, impairment of renal function was essentially equal and ranged from minimal to severe. Furthermore, on occasion, Holley *et. al*[1] have noted moderate or severe atheromatous disease of the renal arteries at necropsy or on arteriograms obtained for other purposes in normotensive patients. Such lesions are usually bilateral and most often located in the proximal portion of the artery adjacent to the aorta. With this in mind, it becomes clear why assessment of the significance of bilateral lesions and the selection of patients for surgical intervention have proved decidedly more difficult than in the unilateral case.

These two facts: difficulties encountered in predicting the response of hypertensive patients to surgical correction of bilateral atheromatous renal artery stenosis, and the observation that normotensive patients also suffer from atheromatous lesions of the renal arteries, makes it obvious that more clinical pathological information is needed to determine the frequency and severity of renal artery stenosis, of aortic atherosclerosis, and of renal arteriolar sclerosis in an unselected group of patients. Such information is of the utmost importance if we hope to elucidate the relationship of these conditions to hypertension.

Holley, *et. al.* found 295 micropsies available for analysis, 256 were on normotensive and 39 on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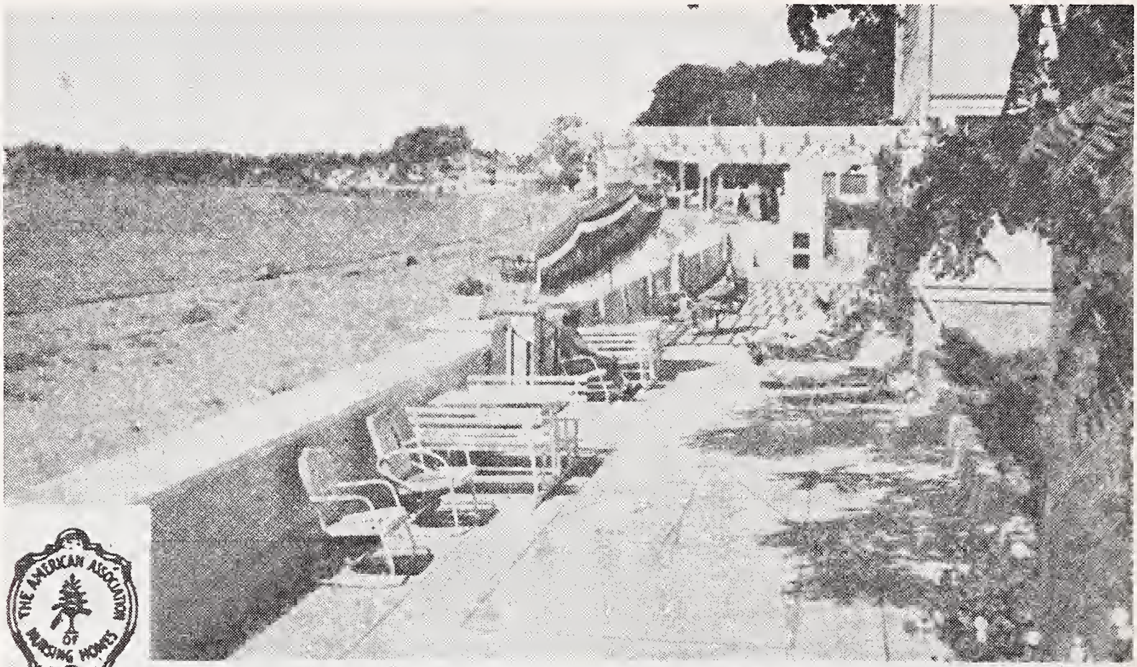

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hypertensive patients. In the normotensive cases they found 130 with minimal, 82 with moderate and 44 with severe renal artery stenosis. In the thirty-nine hypertensive cases the degree of involvement of the renal arteries was minimal in nine, moderate in eight, and severe in twenty-two. In all instances stenosis of the renal artery was caused by atheromatous lesions which was diffuse but selectively located in the proximal one-third of the renal artery. Furthermore, a similar proportion of atherosclerosis was found in both normotensive and hypertensive patients. What is more astonishing is that these authors found that the kidney itself did not reveal any clue as to the existence of hypertension or normotension in the patient from whom they were obtained.

It is clear from the present study that moderate or severe renal artery stenosis is by no means confined to patients with hypertension. The etiologic significance of renal artery stenosis however is greater in hypertensive patients under fifty years of age than in those over fifty. Arteriolar changes in the kidney were found to be more closely related to hypertension than were renal artery lesions, but the former may be secondary to and not the cause of hypertension.[2]

The clinician can learn from such studies that multiple or aberrant renal arteries are found equally between patients with and without roentgenographic evidence of renal artery disease.[3] He can learn also that the degree of atherosclerosis was essentially the same in normotensive and hypertensive patients when patients fifty years old or over were considered. In this group moderate or severe atherosclerosis was present in eighty-two per cent of the normotensive and in ninety-one per cent of the hypertensive patients. For the roengenologist, the study reveals the accuracy of his method in properly visualizing the renal arteries and detecting the existence of stenosis.

From the study, it would appear that demonstrations of bilateral or unilateral renal artery stenosis does not warrant the conclusion that the stenosis is responsible for the associated hypertension. This is particularly true in patients who are over fifty years of age. One must undertake ancillary studies to determine the clinical significance if any, of the renal artery stenosis before appropriate decision regarding surgical management can be reached. Among many methods utilized for this purpose are excretory and retrograde urography, renal function studies of individual kidneys following ureteral catherization and the use of isotope labelled substances for external counting over separate kidneys. These of course are besides renal angiography which while permitting excellent visualization of the renal vascular anatomy, does not by itself establish the functional significance of stenosing lesions. This is especially true in patients over fifty.

One real question raised by Holley's data is why many patients with renal artery stenosis are normotensive. Can it be that kidneys secrete a hypotensive as well as a hypertensive humoral agent and therefore can maintain a normal arterial pressure in the presence of renal artery stenosis? If so, what can this substance be? If the kidneys can antagonize hypertension how do they do it, with what means and why does it operate in some and not other patients with renal artery stenosis? As is true in all scientific progress, the answer to one question leads to many others still to be answered.

L.H.N.

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Progress In Antiviral Therapy

In the past decade there has been remarkable progress in our knowledge of viruses pathogenic to man. This has occurred largely through the development of in vitro cell culture techniques and it is now possible to grow in the laboratory many viruses whose existence could be only inferred because of the specific diseases which they produce for example, measles, German measles, chickenpox, small-pox, adenoviruses and common cold viruses. In addition, the same techniques have allowed for recognition of a number of agents previously unknown for which diseases in human beings have been sought, such as ECHO viruses (Enteric cytotoxic human Orphan) and reoviruses.

Because of the present biochemical orientation of current biologic research, viruses have been separated into two basic forms, those containing DNA such as the poxes and the Herpes viruses and RNA such as influenza, mumps, measles, polio, Coxsackie and ECHO viruses. This in turn undoubtedly must soon lead to chemical attack upon them.

Because of our ability to grow the viruses, we now have an understanding of the evolution of the infections in animals and man. Late in the incubation period there is massive viremia before the clinical picture of fever and localization takes place and while the patient is still well. In many the pharyngeal secretions are positive during the first week of illness and the feces sometimes continue to be positive for a month or longer. It is during the incubation period, that distal foci such as the meninges are seeded and it is during this period that our best hope exists at present for preventing a serious illness.

Having been able to isolate and propagate the offending virus and having thereby been able to study the stages of infection in the human, it is not surprising that we are entering the era of the conquest of virus diseases, not merely by vaccines as a prophylactic measure, but by curative procedures as well. The most striking advance in knowledge besides the production of vaccines has been in the use of drugs in the prevention and therapy of virus diseases of which currently four different types of drugs are undergoing study: immune globulin, IDU., Thiosemicarbazone and Interferon.

Immune globulin and especially hyper-immune gamma globulin (HIGG) is growing in use and methods of preparation. Its use is based upon the concept that viremia which occurs late in the incubation period is responsible for both the fever and the skin eruption which often accompanies it. Hyper-immune gamma globulin is prepared from plasma taken from donors four to eight weeks after successful vaccination. Kempe[1,2] conducted trials in India during an epidemic of small pox. Among 75 control contacts, nine contracted small pox and three of these died, while among 56 contacts treated with HIGG only two mild cases occurred. There have been similar striking results in protecting infants with eczema against eczema vaccination. HIGG has also been used in the prevention of post-vaccinial encephalitis in the Netherlands.

IDU treatment is based upon the knowledge that certain viruses contain DNA of which both vaccinia and variola viruses are examples. Experimental keratitis due to vaccinia has been treated successfully with IDU. IDU prevented successful vaccination[3] and therefore cannot be used to minimize effects of vaccination. Furthermore, its toxicity may well prove a major limitation of the usefulness of this agent for anything other than topical application.

The Thiosemicarbazone compounds have been investigated as potential protective agents for vaccinia and variola infections since 1951. A field study of one such compounds in the prophylaxis of small pox in India yielded significant results.[4] Household contacts were treated with a derivative (Marboran) by mouth for one to four days. Only three mild cases of small pox occurred among 1,101 treated contacts, as compared to 98 cases with 12 deaths among 1,126 untreated contacts. Furthermore the drug had a prophylactic effect even when given late in the incubation period when there is a massive viremia. The results of attempts to treat active small-pox with Marboran are only equivocal. The experience with this drug, however, is still limited and recommendations for its use must await further trials.

The fourth growing area of attack upon viruses is Interferon. The interaction of a virus and a cell results in the production of a protein called Interferon which when applied to other cells makes them resistant to viral infection.[5,6] Production of Interferons may be stimulated by non-infective nucleic acids as well as by attenuated and fully virulent viruses. Interferon has recently been demonstrated in body fluids during the course of human viral infections.[7]

Interferons are small proteins (20,000-30,000 molecular weight) relatively resistant to heat and pH changes, and they are weakly antigenic. They act intracellularly to interfere with the syntheses of infectious virus, whereas serum antibody inactivates the virus extracellularly. For this reason Isaacs and Hitchcock[5] believe that the physiologic role of Interferon is to produce recovery from viral infection. In humans infected with vaccinia, 24 of 28 volunteers showed partial protection from Interferon, while eight showed complete protection at the challenge site. When Interferon was applied topically at intervals of half an hour to the eyes of six patients suffering from vaccinial keratitis it apparently led to rapid symptomatic relief and corneal epithelium healed in one to four days. There will undoubtedly be further studies delineating the efficacy of this material.

Aside from hyperimmune gamma globulin currently recommended for treatment of susceptible contacts and for the complications of vaccination, the other drugs are still in the stage of clinical investigation. None of them can take the place of vaccination. IDU may be used for ocular complications. Experience with Marboran is limited and recommendations for its use must await further trials. Interferon, though extremely promising must await further experiences and is not yet ready for general clinical use.

Virologic research can be expected to result in the development of new antiviral compounds. But as was seen above, viruses differ in structure and effective viral chemotherapy will require greater emphasis on rapid and accurate diagnostic methods. There are still a number of important disease producing viruses that remain to be grown in the laboratory: hepatitis, infectious mononucleosis and of course tumor viruses head the list. Let us hope that the next decade will see the solution of protection against viral disease including tumors.

L.H.N.

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William Shakespeare And John Hall

Of particular interest to physicians in this four hundredth anniversary year of the birth of William Shakespeare is the fact that his eldest child Susanna was married to John Hall, a prominent practitioner of Stratford.

John Hall was born in Bedfordshire in about 1575. His father was a man of considerable means and property, and he and his brother Dive attended Cambridge. He received a bachelor of arts degree in 1593 and a master's degree in 1597. The details of his medical education are obscure. It has been stated that he received some medical training at the University of Montpellier, but he is not listed in its register for that period. There is no actual evidence of his having received a degree in medicine or a license from the Royal College of Physicians or church authorities at any time. He came to Stratford in about 1600, and became a successful and popular practitioner.

Hall was active in church and civic affairs, and in both he showed the strength of conviction and tenacity in holding to unpopular opinions that he exhibited in regard to his sometimes unorthodox therapy. He was elected Burgess to the City Council of Stratford upon three occasions, but declined the first two elections on grounds of pressure of his practice. When he finally took his place on the Council, he was fined several times for non-attendance, and gave up the post after fifteen months. He held several offices in his church, and was a zealous warden. He was active in the Puritan movement, and became involved in the controversy between the Puritan vicar Thomas Wilson and the Stratford Corporation, which was oriented towards the Church of England. He was Wilsons's chief supporter on a number of issues. He died on November 25, 1635, while fighting a plague epidemic in Stratford.

The relationship of Hall to Shakespeare's medical references has been the subject of much speculation. Simpson,[1] in a careful analysis, finds that the majority of medical references in the plays occurs in those written prior to Hall's arrival in Stratford, and that their quality does not differ from those in the later plays. However, the seven physicians who appear as characters in the plays occur in those written after 1600. They are generally portrayed with dignity, respect, and sympathy, and Simpson feels that the precept and example of Hall as a practitioner may have influenced his father-in-law in this regard.

Hall's casebook has been preserved and forms a large part of a recently published work about him by Harriet Joseph.[2] He had a large and diversified practice and treated people of all strata of society and from a large area with competence and consideration. The case reports are short and consist of lucid descriptions of symptoms, details of the elaborate prescriptions of his day, and statements of the results. It is of interest that his treatment for scurvy was a mixture of plant and vegetable juices that actually contained goodly amounts of ascorbic acid. He was censured by his colleagues for this unorthodox therapy, which preceded James Lind's use of lime juice by a hundred years, but held to his opinion with the same tenacity he showed in his controversial dealings with city and church. It is clear that Hall intended his casebook as a guide for practitioners, and this may account for the paucity of failures included. The casebook provides an excellent picture of the activities of a competent seventeenth century English provincial physician, and its reprinting in Mrs. Joseph's volume is a welcome event in this anniversary year.

H.L.

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Of Blindness And Braille

Blindness and braille are often synonymous both to ophthalmologists and their patients. To the doctor braille suggests a practical means of reading and writing when eyesight fails, a skill which could be learned by partially sighted persons in preparation for increased loss of vision. To the patient braille means only blindness. The doctor's suggestion that he learn it is an announcement that he will be blind. His acceptance or rejection of braille reflects his subjective acceptance or rejection of blindness itself. To the public, too, braille and blindness are one, a menacing, fearful combine.

Braille is an ingenious system based on a cell of six raised dots, three dots high, two wide. From combinations of these, sixty-three different characters are possible. Each symbol is assigned a meaning, a number, a letter or group of letters, punctuation sign, etc. Thus braille can depict a musical score, mathematical problem, chemical formula and any spoken language. In languages wherever possible, equal signs are used for equal sounds. The braille system was developed in France by Louis Braille. Its alphabet became known in the United States by 1830. It is now universally the most widely used method of embossed communication.

When hand scribed, the raised dots are made by use of an aluminum slate with equi-spaced cell openings through which one punches inserted paper against a hollowed back plate with a pick shaped stylus. Each symbol has to be reversed and writing done from right to left so that when the paper is turned the dots will be raised and read from left to right. Braille writers with six keys, one for each dot, are compact, typewriter-like devices on which braille can be rapidly and mechanically embossed, right side up.

Mastery of braille for facile touch reading requires memorization of the actual dots used in each symbol, visualization of its shape, and sensitivity of touch. To learn braille by sight does not enable one to read it if blind. Braille is slow for the newly-blinded adult with undeveloped sense of touch, and impossible for some diabetics and others whose touch is impaired. The gist of the printed material is often dissipated by the concentration required to recognize each word. In most published braille, words are not spelled out but are built up of contractions.

Blindness and braille are not synonomous. Indiscriminate prescription of braille kills more often than it cures. Fear of it, aversion to it or disciplined determination to learn it for no realized purpose, distorts and compounds the problem of blindness. Feelings of guilt or failure too frequently follow inability to memorize the symbols or to actually discern the tiny dots. Braille should never be inflicted by direction or inference. Its usefulness is limited by its users.

More than half of all blind people are adults over sixty. This proportion promises to increase as more people live longer. The predominant causes of blindness are now degenerative in origin, many of which entail other disabling infirmities. Most older blind people neither need nor want braille.

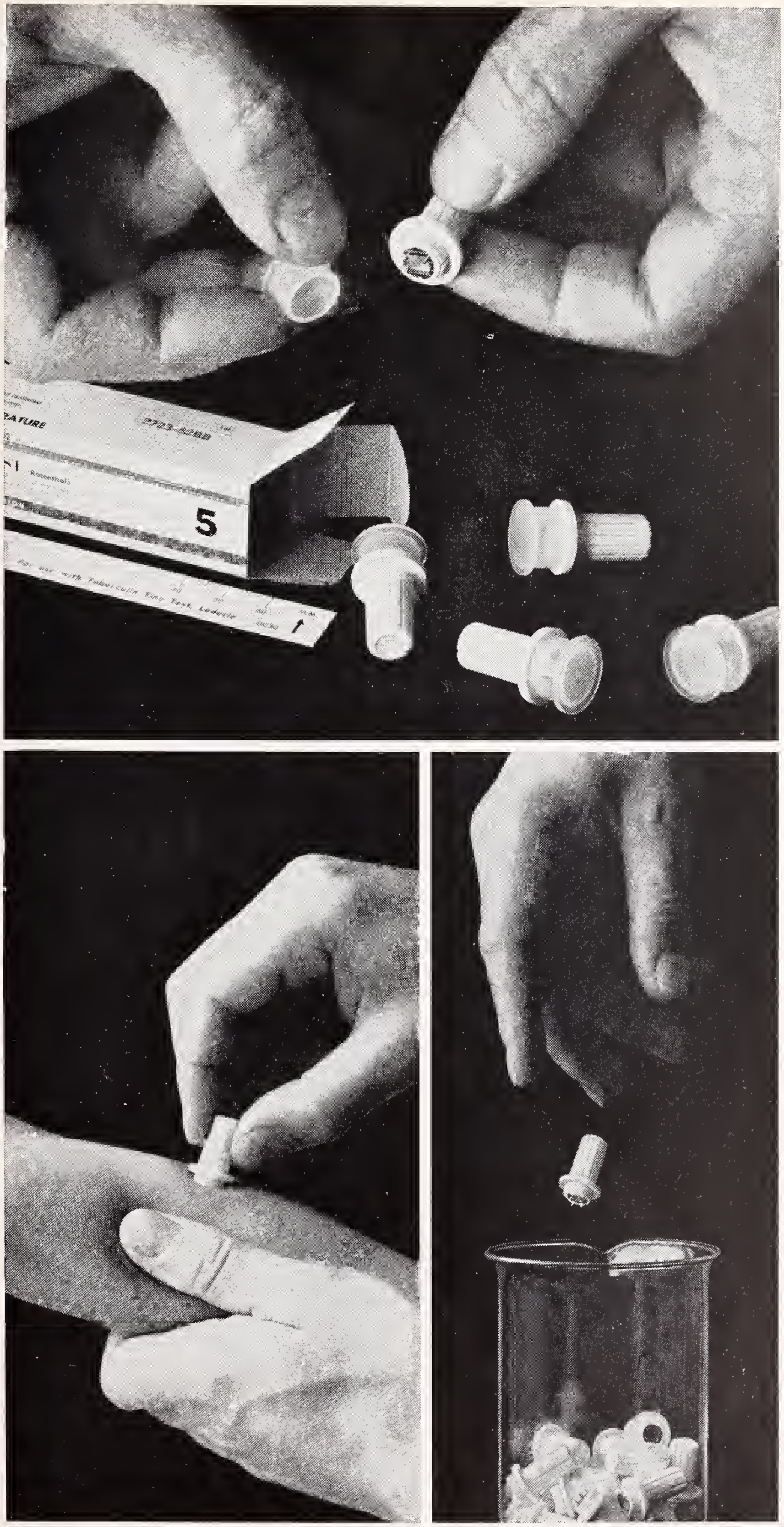
Among younger people, those who can distinguish large print are encouraged to do so. Braille is taught both in public schools where blind students are integrated, and in special schools exclusively for blind children to all those who cannot see print.

Newly-blinded adults, whose vocational objective requires record-keeping, note-taking or calculation need braille. Some home-makers use simple braille for recipes, telephone numbers, grocery lists. In each instance the use to which braille is to be put determines the amount to be learned and fosters the motivation for its attainment.

Reading by sight is the most rapid method. Reading by ear is the next most satisfactory way. Thousands of recorded books and periodicals as well as the machines on which to play them are provided free to blind readers by the government. The Board of Education and Services for the Blind arranges for their use on the basis of ophthalmological reports verifying legal blindness or the patient's visual inability to read print. Talking books are pleasingly voiced and clearly enunciated. Blind readers can manipulate the record players easily, halt or replay, control volume and tone at will. Earphones are supplied for individual use if the regular speaker is inadequate or its sound undesirable to others. For most blind persons, therefore, recorded reading is preferable to touch reading. They augment it by use of radio and television for current news, information, commentaries and "on the spot" broadcasting of special events.

We whose profession it is to work with blind people must tailor rehabilitation counselling and instruction to the temperament, the abilities, and the needs of each individual, whether congenitally or adventitiously blind, child, adult or aged. Our goal is to reinforce each person's ability and self-confidence with useful techniques that he function as independently as possible within the framework of his values and his peers. Perhaps he can read print with magnification. Perhaps he will choose from the increasing resource of large print materials. Perhaps he will listen to talking books. Or, perhaps, he will be the rare one out of ten who reads braille.

JEAN W. ANDERSON, A.B., M.A.
Supervisor of Home Teachers
Board of Education and Services for the Blind.



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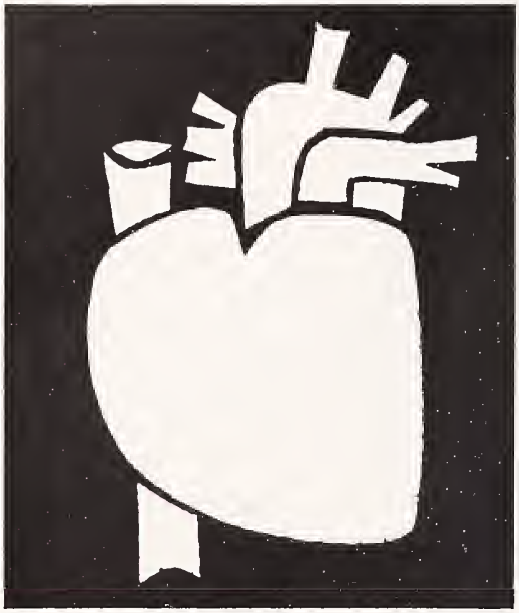

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meprobamate 200 mg. + pentaerythritol tetranitrate 10 mg.

IN ANGINA PECTORIS AND CORONARY INSUFFICIENCY

Provides long-term coronary vasodilation[1-11, 16]
Plus long-term control of anxiety in heart disease[12-16]

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Indications: 'Miltrate' is useful for prophylaxis of pain in angina pectoris and coronary insufficiency, especially where anxiety is a factor. **Contraindications:** Like all nitrates, pentaerythritol tetranitrate should be avoided or prescribed cautiously for patients with glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use. **Precautions:** *Meprobamate* —Patients engaged in activities requiring alertness should be warned of drowsiness. Meprobamate may increase the effects of excessive alcohol, and the possibility of dependence should be considered, particularly in patients with a history of drug or alcohol addiction. Sudden withdrawal may result in reactions, rarely epileptiform seizures. Grand mal attacks may be precipitated in persons susceptible to both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies. **Side effects:** *Pentaerythritol tetranitrate* —The most common side effects are transient headache, nausea, and rash. Weakness, palpitation, flushing, gastrointestinal distress, and lightheadedness have been reported on a few occasions. *Meprobamate* —May cause drowsiness and, rarely, ataxia, usually controlled by decreasing the dosage. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses of the drug. Mild reactions include urticarial or maculopapular rash. Serious reactions, rarely encountered, include dermatological effects, acute nonthrombocytopenic purpura, chills, fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises, anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic, and the drug not be reinstituted. **Dosage:** Usual dosage is one or two tablets before meals and at bedtime. Individualization of dosage is required for maximum therapeutic effect. Doses above twelve tablets daily are not recommended. **Supplied:** White tablets, each containing meprobamate 200 mg. and pentaerythritol tetranitrate 10 mg. *Before prescribing, consult package circular.*

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Incidence Of Peptic Ulcer In 100 Allergic Patients During Long-Term Corticosteroid Therapy

Henry Sherwood, M.D., Joseph I. Epstein, M.D., and Harry Kaplan, M.D.

■ In 1960 two of the authors[1] reported on the incidence of peptic ulcers in 24 allergic patients treated for 68-114 weeks with specific desensitization plus corticosteroids. Serial X-rays of the gastrointestinal tract were performed four times during that study. From that report it seemed that triamcinolone* administered orally was less ulcerogenic than those steroids previously available. It was felt, however, that 24 patients were insufficient for statistical purposes. This paper is an extended report of 76 additional patients treated for one to five years on daily maintenance therapy, with all patients being X-rayed at the end of the study.

The observations to be presented suggest that triamcinolone in doses not exceeding 6 to 8 mgms daily, orally can confidently be continuously administered for periods up to 276 weeks with the assurance that the risk of peptic ulcer formation is negligible.

Selection Of Patients: Method Of Treatment

The patients, 39 males and 61 females (ages 18 to 79 years), were taken from our private practice and from the outpatient allergy clinic of the Institute of Allergy, Roosevelt Hospital, New York City. The patients selected for this study were those who could not be symptomatically controlled with the usual modalities including desensitization therapy at the time this study was initiated. Since then 52 patents have been able to stop steroid therapy and are controlled. Their allergic conditions, usually of long duration, were complicated by emphysema, hyperplastic and purulent sinusitis, pulmonary fibrosis, and chronic purulent bronchitis. All patients had complete histories taken, including physical examination, skin testing, X-rays of lungs and sinuses, and any additional laboratory work required for proper diagnosis.

Triamcinolone was chosen because (1) its effectiveness was well established,[2-5] and (2) in contrast to older steroids, its use was less likely to result in edema or deposition of excessive fat.[6,7] It was administered at the lowest dosage levels (2 to 8 mgms. daily) required to achieve and maintain satisfactory symptomatic control and was continued for periods which extended from 84 to 276 weeks (1½-5¼ years). (These dates are summarized in Table I.) It was found that the daily requirement could be administered as one dose either in the morning or evening with the same effectiveness as when given twice or three times daily. No adjunctive medication for ulcers was given, with the exception of antacids to two patients with active duodenal ulcers. Twenty-four of these patients had X-rays of the intestinal tract prior to the administration of triamcinolone and all patients had an upper gastrointestinal series (barium meal) at the completion of the study. Fluoroscopy was performed and spot films were taken routinely. All patients were under active desensitization therapy during this study. They were seen weekly at first then every second week while the study was in effect. All side effects were carefully noted. Patients were encouraged to report any gastrointestinal symptoms or tarry stools between visits.

Peptic Ulcers Before Treatment

Because of the possibility of side effects arising from this long-term steroid regimen, special attention was given to predisposing factors in these

TABLE I

CONDITIONS TREATED; DOSES; LENGTH OF TREATMENT

TYPE OF ALLERGIC DISORDER	NUMBER OF PATIENTS	DURATION OF DISEASE (YEARS)	MAINTENANCE DOSE (M.G./DAY)	DURATION OF THERAPY (WEEKS)
Asthma	48			95-160
		2-54	2-8	
	29			198-276
Perennial rhinitis	12	2-15	2-4	81-252
Allergic dermatoses	11	3-15	2-4	104-158

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* Manufactured as ARISTOCORT® Triamcinolone Tablets by Lederle Laboratories, A Division of American Cyanamid Company.

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patients. Before treatment all had comprehensive medical histories taken. Special care was taken to elicit any gastrointestinal symptoms or family history of diabetes or tuberculosis.

Table II
Peptic Ulcers Before Treatment

NO. OF PATIENTS	NUMBER X-RAYED	NUMBER NEGATIVE	NUMBER WITH ACTIVE ULCERS	NUMBER WITH HEALED ULCERS	ULCER (?)
100	24	17	4	3	1*

* By history only—elicited after an ulcer was found by X-ray at the end of the study.

Of the patients whose ulcers were confirmed by X-ray before treatment, six had duodenal ulcers only and one had duodenal and gastric ulcers. One patient had made no mention of ulcer-related symptoms prior to therapy and therefore had no X-ray studies taken. However, an upper GI series demonstrated a typical duodenal ulcer 152 weeks following start of therapy. When re-questioned, this patient admitted symptoms definitely suggestive of ulcer, which were present two years before treatment with triamcinolone was begun. This case remains in doubt and is more fully discussed at a later point in this report.

Results Of Treatment

Improvement was measured by the following standards:

Good: Asymptomatic—92 patients

Fair: Infrequent symptoms of asthma (non incapacitating) seven patients

Poor: Almost no change from previous status—one patient

Side Effects

Side effects were infrequent, chiefly of Cushingoid type, and never serious enough to cause discontinuation of the drug (Table III). The medication induced no adverse effects in 74 patients.

Acne reactions were not severe and ecchymosis was moderate in three and mild in the remaining four patients. Gastrointestinal symptoms were mild in two patients, one of whom had an active ulcer and required anti-ulcer therapy. The other had no ulcer and required no medication.

Of the two patients who had osteoporosis and spontaneous fractures, one was age 70 and had been bedridden for 10 years prior to the use of steroids. After her course of therapy was begun, she was able at least to care for herself and enjoy a relatively comfortable existence, until bullous emphysema and respiratory acidosis caused her death. The second patient was 55 was a history of lifelong asthma and marked hyphoscoliosis. X-rays taken many years prior to steroid usage had shown moderate generalized osteoporosis.

Table III

SIDE EFFECT	NO.*
Acne	2
Ecchymosis	7
GI symptoms	2
Hirsutism	7
Moon face	13
Osteoporosis	2
Weakness	5
Spontaneous fractures of ribs	1
Spontaneous fractures of spine	1

* There were 38 side effects in 26 patients.

Peptic Ulcers After Treatment

The results of the post-treatment studies are illustrated in Table IV. Ninety-two patients showed no evidence of peptic ulceration. The remaining eight are summarized as follows: Of the four previously active ulcers, three had healed during therapy, while the patient with both gastric and duodenal ulcerations showed arrest of the duodenal but not the gastric ulcer. The three healed ulcers remained quiescent (one did not show up on the roentgenogram). The last of the eight patients, in whom an active ulcer was observed at the end of her course of treatment, should probably be considered as representing the only instance of steroid-induced ulcer in this series. However, evidence of symptoms existing prior to treatment was discovered at the close of the study. None of the ulcerations led to hemorrhage or perforation.

Thus, active or healed ulcers existed *prior to treatment in seven* or *eight percent* (depending upon the questionable case) of the patients. *Following treatment* periods of 1-5 years, active or healed ulcers were demonstrated in seven per cent of the patients, including one probably related to the administration of triamcinolone.

An examination below of some of the less widely heralded investigations shows that these findings are not inconsistent with those of other clinicians.

Discussion

INCIDENCE OF PEPTIC ULCER IN UNTREATED POPULATIONS

The incidence of peptic ulcers in the population-at-large has been placed at figures which range from 5 to 10 per cent. Gray,[8] at the upper end of the scale, estimates that between 1.5 and 4.5 million people each year are subject at some time to peptic ulcer. Thus, the seven or eight per cent *pretreatment* figure in the patients investigated in the present study indicates that this group may be considered representative for purposes of comparison.

Table IV
Profile of Patients with Peptic Ulcers

PATIENT	AGE/SEX	ULCER STATUS BEFORE TREATMENT	DOSE OF TRIAMCINOLONE (MG./DAY)	DURATION OF TREATMENT (WEEKS)	ULCER STATUS AFTER TREATMENT
K.O.	36/F	Active Duodenal Ulcer	4-6	140	Healed Duodenal Ulcer
O.O.	66/M	Active Duodenal and Gastric Ulcers	4-8	104	Healed Duodenal and Active Gastric
J.B.	52/F	Healed Duodenal Ulcer	2-4	114	Healed Duodenal Ulcer
L.G.	50/F	Active Duodenal Ulcer	4-6	102	Healed Duodenal Ulcer
J.K.	51/F	Healed Duodenal Ulcer	4-6	198	No Evidence of Ulcer
H.L.	55/F	Healed Duodenal Ulcer	3	160	Healed Duodenal Ulcer
A.H.	48/M	Active Duodenal Ulcer	3	104	Healed Duodenal Ulcer
E.R.	44/F	Ulcer by History Only	4	152	Active Duodenal Ulcer

INCIDENCE OF PEPTIC ULCER IN STEROID-TREATED POPULATIONS

In many studies incidence of ulcers in steroid-treated patients does not vary significantly from that of the "normal" population. Rees,[9] for example, who used *minimal doses of various steroids* for periods up to seven years in 317 patients with asthma, found an incidence of 1.9 per cent new ulcers demonstrated by repeated radiologic studies. There were no perforations and only two hemorrhages, which suggested to the author that "with care, the complication of peptic ulceration in steroid therapy need not be a serious risk." Arnoldsson,[10] using barium-meal examinations at intervals of four months, observed 5.3 per cent new peptic ulcers in asthmatic patients receiving various steroids, and 5.0 per cent upon single examination in untreated asthmatics. In another study 47 patients were given triamcinolone in varying doses for rheumatoid arthritis. Of the 23 who were placed on a maintenance regimen of *6 mg. or less,* only three suffered slight discomfort and all continued to be well maintained with much better responses than at equivalent doses of prednisone or prednisolone.[11] A tabulation, compiled by the American Rheumatism Association, of 564 patients receiving steroids, revealed that overall incidence of peptic ulceration was 6.6, per cent, *4.4 per cent in those receiving less than 50 mg. cortisone per day* and 8.3 per cent in those on more than 50 mg. per day.[12] In other reports, where the common denominator was the *relatively low doses* of various steroids employed, the incidence of ulcers ranged from 0 to 7.8 per cent.[13] These figures are well within range of the normally expected incidence in *untreated* populations. In contrast, in studies where larger doses were used, evidence of ulcers rose to as high as 47.0 per cent.[13]

These and other studies point to the conclusion that the degree of ulcerogenic potential of steroids is to a large extent related to the amounts administered, although there are undoubtedly other factors too. Brown and Haserick[14] concluded: "In general peptic ulcer develops more frequently in those patients who have been given *large doses* of steroids for relatively long periods of time." They found that even in patients with histories of previous ulcers, steroids can be safely given when combined with routine ulcer treatment.

Results of our earlier studies indicated that triamcinolone was less likely to induce ulcers at doses equivalent in anti-inflammatory activity to hgher amounts of other corticosteroids. In allergic conditions triamcinolone was equally as effective as prednisone at approximately one-half the dose.[15] (For other conditions, however, the ratio is usually considered 4 mg. triamcinolone to 5 mg. prednisone.) Because of the potency of this drug in allergic diseases, doses could be maintained at levels sufficiently low to prevent serious complications while sustaining the necessary beneficial effects.

Summary

A study was designed to evaluate triamcinolone on two levels. First, is it effective in small doses in refractory allergic diseases? Second, can it be given safely for long periods; will it induce the formation of an alarming number of peptic ulcers?

Patients with allergies chiefly of respiratory origin were started on a regimen of triamcinolone—after all other measures had failed—in doses aver-

aging 5 mg., a day for periods up to 276 weeks. Satisfactory relief of symptoms was obtained in 99 of 100 patients treated. A variety of side effects, none serious enough to cause withdrawal of the drug, occurred in 26 patients. Roentgenographically four active and three healed ulcers were found prior to the start of therapy. At the end of the period of observation four duodenal ulcers had healed by X-ray. In the one patient who had both a gastric and a duodenal ulcer, the duodenal ulcer had healed, the gastric ulcer was the same, still active. It is believed that one duodenal ulcer found by X-ray after treatment was related to the steroid, although there was evidence to indicate that prior symptoms had existed in this patient, but not elicited at the time she was placed in this study. These findings suggest that triamcinolone in oral doses up to 6 to 8 mg. daily can be used for prolonged periods with little danger of ulcer formation.

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APPENDIX

SUMMARY OF 100 PATIENTS TREATED

PATIENT	AGE/SEX	DIAGNOSIS	AVERAGE DOSE (MG./DAY)	LENGTH OF TREATMENT (WEEKS)	X-RAY BEFORE TREATMENT	X-RAY AFTER TREATMENT	SYMPTOMATIC CONTROL	SIDE EFFECTS
E.A.	50/F	Asth., C.H.S., P.R.	2–4	200	None	Negative	Good	None
E.A.	24/F	Asth., Emph.	8	100	Negative	Negative	Good	Moon face, Acne, Hirsutism, Ecchymosis
J.B.	52/F	Asth., C.H.S.	2–4	114	Healed duodenal ulcer	Duodenal ulcer crater	Good	Weakness
N.B.	79/F	C.H.S., P.R., R.A.	2	252	None	Negative	Good	None
M.B.	51/F	Asth., C.H.S., P.R.	4	84	None	Negative	Good	None
D.B.	38/F	Asth., C.H.S., Empt.	4–6	156	None	Negative	Poor	Moon facies, Ecchymosis
M.B.	49/F	Asth., P.R.	2–4	104	None	Negative	Good	None
J.B.	42/M	P.R.	2	104	None	Negative	Good	None
R.B.	63M/	A.E., Asth., C.H.S., Emph.	8	104	Negative	Negative	Good	None
R.B.	65/M	Asth.	4	200	None	Negative	Good	None
R.B.	37/M	Asth., C.H.S.	4	250	Negative	Negative	Good	None
L.B.	72/F	Asth., Emph.	3	104	None	Negative	Good	None
P.B.	30/F	C.H.S., C.U., P.R.	2–4	250	None	Negative	Good	None

APPENDIX (CONTINUED)
SUMMARY OF 100 PATIENTS TREATED

PATIENT	AGE/SEX	DIAGNOSIS	AVERAGE DOSE (MG./DAY)	LENGTH OF TREATMENT (WEEKS)	X-RAY BEFORE TREATMENT	X-RAY AFTER TREATMENT	SYMPTOMATIC CONTROL	SIDE EFFECTS
G.C.	50/M	Asth., C.H.S., Emph.	4–6	260	None	Negative	Good	None
H.C.	43/F	Bact. Id.	2	104	None	Negative	Good	None
J.C.	42/F	Asth.,C.H.S., Emph.	6–8	260	None	Negative	Good	Moon face, Hirsutism Ecchymosis
H.C.	35/F	Asth., C.H.S.	2	250	None	Negative	Good	None
J.C.	36/F	Asth., C.H.S., P.R.	4	156	None	Negative	Good	None
D.D.	50/F	Asth., C.H.S., Emph.	4–6	138	None	Negative	Good	Moon face
D.D.	20/M	C.E.	4–6	104	None	Negative	Good	None
E.D.	55/F	Asth., C.H.S., Emph.	8	260	None	Negative	Fair	Ecchymosis, Hirsutism, Osteoporosis, Rib fractures
G.D.	47/M	C.H.S., C.U.	2–4	100	None	Negative	Good	Minimal weakness
M.D.	37/F	Asth., Emph.	6	198	None	Negative	Good	Hirsutism
R.D.	42/M	C.H.S., P.R.	4	208	None	Negative	Good	None
G.D.	18/F	Asth., C.H.S.	3	96	None	Negative	Good	None
J.D.	32/F	C.E.	2	108	None	Negative	Good	None
V.E.	33/F	Asth., Emph.	6	117	Negative	Negative	Good	None
F.E.	55/M	Asth., Emph.	4–6	116	Negative	Negative	Good	Weakness
J.F.	41/M	Ehth., C.H.S., Emph.,H.F.	4–6	160	None	Negative	Good	None
A.F.	44/F	Asth., C.H.S.,P.R.	3	156	None	Negative	Good	None
G.F.	43/M	Asth., C.H.S.	4	260	None	Negative	Good	None
I.F.	50/F	Bact. Id.	4	114	None	Negative	Good	None
F.G.	41/M	Asth., C.H.S., Emph.	4	260	None	Negative	Good	None
L.G.	50/F	Asth., C.H.S.	4–6	102	Active duodenal ulcer	Healed duodenal ulcer		
L.G.	51/F	C.H.S., P.R.	4	226	None	Negative	Good	None
A.G.	43/F	Asth., C.H.S., Emph.	2–3	104	None	Negative	Good	None
L.G.	36/F	Asth., Emph.	4	236	Negative	Negative	Fair	None
M.G.	32/M	Asth., R.A.	4	104	None	Negative	Good	None
D.G.	49/F	Asth.	4	104	None	Negative	Good	None
J.G.	40/M	Asth., C.H.S.	4	104	None	Negative	Good	None
L.H.	43/F	Asth., C.H.S.,P.R.	4	260	None	Negative	Good	None
R.H.	63/F	P.R.	2	128	None	Negative	Good	None
V.I.	49/F	Asth., C.B., C.H.S., Emph.	8	260	None	Negative	Fair	Moon face Ecchymosis
J.J.	48/F	Asth., C.H.S.	4	116	None	Negative	Good	None
B.J.	63/F	Asth., Emph.	6	156	None	Negative	Fair	Moon face
C.J.	42/M	Asth., R.A.	6	95	Negative	Negative	Good	None
J.K.	65/M	A.E., Asth., C.H.S., Emph	3	124	None	Negative	Good	None
J.K.	51/F	Asth., C.H.S. Emph.	4–6	198	Healed duodenal duodenal	No evidence of active ulcer	Good	Moon face
M.K.	33/F	Asth., C.H.S.	4	208	None	Negative	Good	None
N.K.	38/F	Asth., C.H.S.	4	260	None	Negative	Good	None
E.K.	45/M	Asth., C.H.S.,P.A.	4	208	None	Negative	Good	None
H.L.	55/F	C.H.S., P.R.	3	160	Healed duodenal ulcer	Healed duodenal ulcer	Good	Weakness
R.L.	49/M	C.E., C.H.S.	2–4	104	None	Negative	Good	None
O.L.	48/M	Asth., C.H.S., Emph.	6	127	None	Negative	Good	Weakness
H.M.	49/F	C.E.	4	120	None	Negative	Good	None
M.M.	51/F	Asth., C.H.S.	4	252	None	Negative	Good	None
W.M.	59/M	Asth., C.H.S., Emph.	4–6	276	None	Negative	Good	Ecchymosis
D.M.	38/F	Asth., C.H.S.	4–6	120	None	Negative	Good	None

APPENDIX (CONTINUED)
SUMMARY OF 100 PATIENTS TREATED

PATIENT	AGE/SEX	DIAGNOSIS	AVERAGE DOSE (MG./DAY)	LENGTH OF TREATMENT (WEEKS)	X-RAY BEFORE TREATMENT	X-RAY AFTER TREATMENT	SYMPTOMATIC CONTROL	SIDE EFFECTS
M.M.	39/F	Bac. Id., C.E., H.F., R.A.	4–6	158	None	Negative	Good	Moon face
S.M.	44/F	Asth., C.H.S.	4	104	None	Negative	Good	None
A.N.	47/F	Asth., L.E.	6	120	None	Negative	Good	None
S.N.	46/M	Asth., C.H.S., Emph.	6	260	None	Negative	Fair	Moon face
F.N.	69/M	Asth., Emph.	8	126	Negative	Negative	Good	None
B.N.	56/F	Asth., C.H.S., Emph	4	210	None	Negative	Good	None
B.C.	38/F	Asth., Emph.	4	102	Negative	Negative	Fair	None
A.H.	48/F	Asth.	3	104	Positive	Negative	Good	None
S.O.	34/F	Asth., C.H.S. Emph	2–4	234	None	Negative	Good	None
V.O.	66/F	Asth., C.H.S., Emph.	4	208	None	Negative	Good	None
K.O.	36/F	Asth., C.H.S.	4–6	140	Active duodenal ulcer	Healed duodenal ulcer	Good	Hirsutism Moon face
O.O.	66/M	Asth., Emph.	4–8	104	Duodenal & gastric ulcer-active	Duodenal healed Flare-up of ulcer	Good	?
H.O.	48/F	C.H.S., P.R.	4	260	None	Negative	Good	None
H.P.	74/M	C.E.	2–4	160	None	Negative	Good	None
T.P.	55/M	Asth., C.H.S., Emph.	8	142	None	Negative	Good	Ecchymosis
J.P.	20/F	Asth., C.H.S., H.F.	2–6	160	None	Negative	Good	None
C.P.	32/F	Asth., C.H.S.	4	130	None	Negative	Good	None
F.P.	70/F	Asth., C.H.S., Emph.	4–6	260	None	Negative	Good	Osteoporosis 1 fractured vertebrae Moon face
M.P.	70/F	Asth., C.H.S., Emph.	4	160	None	Negative	Good	None
E.P.	57/F	P.R.	4	200	None	Negative	Good	None
E.P.	46/F	Asth.	4	124	None	Negative	Good	None
J.R.	27/F	C.E., H.F., P.R.	4	198	Negative	Negative	Good	Hirsutism, Acne aggravated
A.R.	69/M	Asth.	3	104	None	Negative	Good	None
J.R.	42/M	Asth., C.H.S.	4	208	None	Negative	Good	None
E.R.	44/F	P.R.	4	152	Ulcer by history only—Active	Positive	Good	Minimal GI symptoms
S.S.	50/F	Asth., C.H.S.	4	104	None	Negative	Good	None
R.S.	28/F	Asth.	2–4	112	None	Negative	Good	None
G.S.	32/F	Asth., Emph.	8	116	Negative	Negative	Good	Moon face, Hirsutism
L.S.	45/M	Asth., Emph.	4	208	None	Negative	Good	None
F.S.	51/M	Asth., C.H.S. Emph.	4	160	None	Negative	Good	None
E.S.	47/M	C.H.S., P.R.	3	108	Negative	Negative	Good	Mild GI symptoms
K.S.	46/F	Asth., C.H.S., Emph.	2–4	156	None	Negative	Good	None
H.S.	49/M	Asth., C.H.S., Emph.	4	248	None	Negative	Good	None
J.S.	45/M	Asth., C.H.S., Emph.	2–4	98	Negative	Negative	Good	None
A.T.	58/M	Asth., C.H.S., Emph.	4–6	104	None	Negative	Fair	None
F.T.	60/M	A.E., C.H.S., P.R.	2	124	None	Negative	Good	None

Acute Appendicitis In The New Haven Standard Metropolitan Area In 1958 And 1959

R. John C. Pearson, M.D.

■ There have been a number of studies of the epidemiological aspects of acute appendicitis, but there has been little emphasis on the incidence of the condition, confirmed by pathological examination, in communities of known size; in fact a review of the literature has revealed only three studies in which attention was paid to this point. Bower[1] reported on cases of acute appendicitis seen in 28 Philadelphia hospitals for the years 1930-1932, and found an average of 3,261 cases a year, or a rate of 1.65 per thousand per year. Six years later Bower[2] reported on the number of cases of acute appendicitis operated upon in 181 of the 186 general hospitals in Pennsylvania in 1937 (of the remaining 5 hospitals 3 had no cases and 2 refused to cooperate); there were 19,398 cases which represents a rate of 1.98 per thousand per year. Watkins[3] reported on a review conducted in Cuyahoga County in which the records of the 16 largest hospitals were abstracted for the 12 years, 1930 through 1941, and an overall rate of 1.2 to 1.4 cases per thousand per year derived. It is not clear, however, in any of these studies how many cases were missed because all the hospitals were not covered, nor how many collected cases occurred in residents of places outside the study areas.

Other surveys measuring incidence did not have data on the pathological findings, and were, more strictly, studies on the incidence of appendectomy. Green and Watkins[4] found the annual appendectomy rate in Cuyahoga County for 1940 and 1941 to be 2.7 per 1,000 persons. Lembcke[5] found the rate for primary appendectomy in the eleven counties of western New York in 1948 to be 3.8, with a range, for the different hospital areas there, between 2.5 and 6.9. Lee et al[6] computed from a 10 per cent sample of the hospital discharges for England and Wales in 1951 that the rate was 2.7 per 1,000 per year. The National Health Survey[7] found a rate of 2.6 per 1,000 per year for the years 1958 through 1960.

All other surveys on acute appendicitis have been surveys of cases seen in a particular hospital,[8–12] or group of hospitals,[13] without reference to the population served; and so incidence rates were not computed.

Method

In this study the incidence rates of acute appendicitis, confirmed by pathologic diagnosis, were computed for the New Haven Standard Metropolitan Area (SMA) for the years 1958 and 1959. The SMA comprises the following nine towns: New Haven, Hamden, East Haven, West Haven, Branford, North Haven, Orange, Woodbridge and Guilford. In the 1960 census,[14] the findings of which are used as the population base, the population of the SMA was 311,681. The data on the cases of acute appendicitis were collected from the following hospitals: the two in New Haven, the Grace-New Haven Community Hospital and the Hospital of St. Raphael; the Veterans Administration Hospital in West Haven; and five hospitals outside the SMA, the Milford Hospital, the Griffin Hospital at Derby, the Middlesex Memorial Hospital at Middletown, and the Waterbury Hospital and St. Mary's Hospital at Waterbury. Ninety-six per cent of the cases were operated upon at the two hospitals in New Haven.

Only those cases were included in which there was positive evidence that the diagnosis was correct. A laparotomy at least had to have been performed, and the excised appendix must have been examined by a pathologist. There were a few cases in which an abscess was found, with or without a necrotic appendix, and in which drainage was the only treatment used; these have been included.

Incidence

There were 378 cases in 1958, and 362 in 1959, occurring in residents of the SMA. The distribution and the rates by different towns are shown in Table I. The rate for the SMA was 1.21 per thousand per year for 1958, and 1.16 for 1959. The range of rates for the individual towns was from 0.75 to 1.77; however none of the rates are statistically different from any of the others.

No attempt has been made to compute an appendectomy rate.

Racial Distribution

In the New Haven SMA, 11 cases in 1958, and 15 in 1959 occurred in non-white persons. The percentage of non-white in the SMA in 1960 was 7.9 per cent. The rates for 1958 were 0.45 per thousand per year for non-white, and 1.28 for white; and for 1959 were 0.61 for non-white and 1.21 for white. The rates for the non-white and for the white are statistically different (S.E. for the difference between the rates for the two years combined = 0.161). ($X^2 = 9.9$; $P < 0.01$ and > 0.001.)

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Table I

Number of Cases of Acute Appendicitis Occurring in Towns in the New Haven Standard Metropolitan Area, (SMA) 1958 and 1959; and Rate per 1000 Population

	1958			1959		
	NO. CASES	RATE	S.E. RATE	NO. CASES	RATE	S.E. RATE
New Haven	201	1.32	0.093	190	1.25	0.091
SMA excluding New Haven	177	1.11	0.083	172	1.08	0.082
Hamden	36	0.88	0.147	41	1.00	0.156
East Haven	28	1.31	0.252	23	1.07	0.233
West Haven	53	1.23	0.168	44	1.02	0.155
Branford	20	1.20	0.267	22	1.32	0.281
North Haven	12	0.75	0.214	18	1.12	0.267
Orange	8	0.94	0.336	10	1.16	0.362
Woodbridge	6	1.15	0.469	5	0.97	0.433
Guilford	14	1.77	0.473	9	1.14	0.380
Total	378	1.21	0.062	362	1.16	0.061

Age Distribution

The age distribution of the cases in 1958 and 1959, and that of the overall population of the SMA in 1960, are shown in Table 2. As can be seen, the age distribution of the cases is similar for the two years. The lowest rate is in the age group 0 to 4 years (0.2 and 0.3 per thousand). The highest rate is in the age group 15 to 24 (2.5 and 2.4), and the next highest in the age group 5 to 14 (2.0 and 2.2).

After the age of 25 the rate is lower; for the age group 25 to 34 it is 1.0, and for the age groups over the age of 35 it varies around 0.7 per thousand per year. The rates for the age groups 0 to 4, 5 to 14, 15 to 24 and over 25 years are all significantly different from each other, and from the average rate for all age groups.

Sex Distribution

With the cases for 1958 and 1959 combined, there were 440 males and 300 females for a ratio of 60:40.

Table II

Incidence Rates of Acute Appendicitis in the New Haven SMA in the Years 1958 and 1959, by Age Groups

	1958		1959			
AGE GROUP	CASES	RATE*	CASES	RATE*	AVER. RATE*	S.E.
0- 4	7	0.2	10	0.3	0.27	0.093
5-14	106	2.0	119	2.2	2.06	0.196
15-24	111	2.5	97	2.4	2.47	0.245
25-34	42	1.0	41	1.0	1.04	
35-44	35	0.8	36	0.8	0.76	
45-54	29	0.8	19	0.5	0.62	0.065
					0.78	
55 64	24	0.8	21	0.7	0.76	
65-	24	0.7	19	0.6	0.65	
Total	378	1.21	362	1.16	1.17	0.061

* Rate by 1000 population.

Table III

Total Cases in the New Haven SMA, 1958 and 1959 Combined, by Age and Sex: Also Rate Per 1000 Per Year, by Age and Sex

	MALE		FEMALE	
GROUP	CASES	RATE	CASES	RATE
0- 4	9	0.28	8	0.25
5-14	129	2.4	96	1.8
15-24	127	2.9	81	2.0
25-34	58	1.5	25	0.6
35-44	43	1.0	28	0.6
45-54	30	0.8	18	0.4
55-64	24	0.9	21	0.7
65-	20	0.7	23	0.6

The population of the SMA in 1960 was almost equally divided (152,911 male: 158,770 female). The rates by sex were 1.44 for males and 0.95 for females; these rates are highly significantly different (S.E. diff. 0.0876; $X^2 = 32.0$, $P < 0.001$).

When the sex distribution is considered by age groups, as in Table 3, it can be seen that at the extremities of life (0 to 4 and over 65 years), the sexes are more nearly equally represented, and that the most marked difference is in the age group 25 to 34.

Seasonal Variation

As noted by Bowers[13] and others, no consistent pattern of seasonal variation could be demonstrated.

Rate Of Complications

As in the Cuyahoga County study[3] the cases were divided into i) uncomplicated cases, ii) cases complicated by perforation, iii) cases complicated by abscess, and iv) cases complicated by both perforation and abscess; it was not considered feasible to compare rates of gangrene and peritonitis from different hospitals.

The findings in this study, shown in Table IV, reveal 149 complicated cases in a total of 740 for the two years combined, for a rate of 20.1 per cent. Perforation alone occurred overall in 64 per cent of the complicated cases, abscess alone in 14 per cent, and both together in the remaining 22 per cent. When the totals are broken down into broad age groups it will be seen, in Table V, that the rate of complications is much higher in the very young,

Table IV

Number and Per Cent of Complicated Cases of Acute Appendicitis in New Haven SMA, 1958 and 1959

YEAR	PERFORATION	ABSCESS	BOTH	COMPLICATED CASES	TOTAL CASES	PER CENT COMPLICATED
1958	58	5	13	76	378	20.1
1959	37	16	20	73	362	20.2
Total	95	21	33	149	740	20.1

TABLE V

NUMBER AND PER CENT OF COMPLICATED CASES OF ACUTE APPENDICITIS IN NEW HAVEN SMA, 1958 AND 1959 COMBINED, BY AGE GROUPS

AGE GROUP	PERFORATION	ABSCESS	BOTH	COMPLICATED CASES	TOTAL CASES	PER CENT COMPLICATED
0- 9	20	7	5	32	112	28.6
10-39	27	9	13	49	461	10.6
Over 40	48	5	15	68	167	40.7
TOTAL	95	21	33	149	740	20.1

and in those aged over 40 years than in the intermediate group. More than one fourth of those aged under 10 years, and more than two fifths of those aged 40 and over had one of these complications. The differences in these rates by age groups are significant. ($X^2 = 59.8$; $P < 0.001$.)

Mortality

In this series there were two deaths, one in 1958 and one in 1959. One was a 73 year old woman who died with peritonitis, septicemia and pulmonary edema after appendectomy for a perforated appendix. The other was a 49 year old man who, following vagotomy for a chronic duodenal ulcer seven days previously, perforated his appendix preoperatively and died immediately after appendectomy with aortic thrombosis. The mortality rate may therefore be computed at 3 per thousand cases; however since there were only three deaths in over 1500 cases in Southern Connecticut whose charts were reviewed, the rate may also be computed at 2.0 per thousand cases.

Discussion

It is unfortunate that there is no conclusive evidence of a trend in the frequency of occurrence of acute appendicitis. Bothe[15] and Castleton[16] both felt that there was a definite decrease in incidence, but their evidence is not completely convincing. This paper also does not settle the question but it may be useful for future comparison. One finding of interest in this study was that each of the hospitals in New Haven and West Haven dealt with a similar number of cases of acute appendicitis each year:

There is however clear evidence that both the rate of complications[1, 2, 10, 17, 18, 19] and the mortality rate[10, 12, 19, 20, 21], which had decreased sharply during the 1920s and 1930s, have levelled off since then.

	1954	1955	1956	1957	1958	1959	AVG.	AVG. 1958/59
Hospital A	—	204	211	203	220	215	211	218
B	—	—	—	—	141	134	138	138
C	13	18	16	26	17	13	17	15
TOTAL					378	362	366	371

The etiology of acute appendicitis is still puzzling. The commonest cause is generally considered to be obstruction of the lumen followed by inflammation distally. The obstruction may be due to fecolith, hyperplasia of the lymphoid tissue, stenosis, kinking, or to a foreign body such as pinworms. Two commonly used textbooks of surgery, Harkins et al[22] and Guis,[23] state that 90 per cent and 80 per cent, respectively, of all cases have one or another kind of obstruction. One of their sources is Bowers[13] who had 80 per cent of his 485 cases with obstruction, and 67 per cent of his cases obstructed by fecoliths. However Koster and Shapiro[24] found fecoliths in 41 per cent of their cases of acute appendicitis and in 57 per cent of the normal appendices that they studied. In this study, in the hospital in which over 50 per cent of the cases were operated upon, fecoliths were found in 14 per cent of the normal appendices, in 15 per cent of the cases of simple appendicitis and in 26.5 per cent of the complicated ones; the impression is therefore reached that fecoliths, at any rate in the experience of this hospital, are not a major cause of obstruction in acute appendicitis. As regards stenosis, kinking and hyperplasia of the lymphoid tissue, no data were collected in this series. Only one child had pinworms in her appendix.

One avenue for exploration lies with viral cultures. It has long been recognized that acute appendicitis is a complication, albeit an uncommon one of measles. In addition, epidemics of acute appendicitis have been reported.[25] On the other hand Zbitnew[26] failed to demonstrate a viral etiology in 31 cases. He may however have tried on the wrong appendices. There was noted in this study, in addition to cases of mesenteric adenitis in the presence of normal appendices, certain cases where mesenteric adenitis was found in the presence of appendices which were acutely inflamed but which were not complicated by perforation or abscess. It is possible that there may have been a viral etiology in these cases, though it is conceded that these cases may also be considered to substantiate Sahli's theory[27] and be similar to acute tonsillitis with cervical adenitis. It may seem worthwhile, at any rate, to a surgeon confronted by these findings to take viral cultures.

What other possible leads are opened up by this study for a greater understanding of this disease? Certainly there seems to be more acute appendicitis in white persons than in negro. This was noted also by Boyce.[28] In addition Dawson quotes Russell as having seen no cases in 17 years of work with the American Indians.[25] Is this because of anatomical differences in the bore of the appendix or in the angle of insertion into the cecum? This could be investigated by comparison of appendices excised for acute inflammation with those excised for other reasons. Or is it because of a difference in the diet? In this connection Dawson[26] reports an epidemic that occurred in American soldiers on a Pacific island after a consignment of food arrived from home.

This could be investigated by careful dietary histories of patients with acute appendicitis. If such a survey did show any common factors during the period before onset, then this would perhaps be a demonstration of a way by which the frequency of the condition could be cut down.

Summary

The incidence rate of acute appendicitis, confirmed by pathologic diagnosis, in residents of the New Haven Standard Metropolitan Area for the years 1958 and 1959, was 1.21 and 1.16, respectively, per 1,000 population per year. These rates are identical with those found by Watkins in Cuyahoga County for the years 1930 through 1941, but are lower than the rates found in Philadelphia, 1929 through 1932, and Pennsylvania in 1937.

There were statistical differences found in the frequency of occurrence of the condition, by race, by sex and by age. In addition, complications were found to be more frequent in the young and the old.

The best hope for diminishing the frequency of the illness seems to lie in finding a dietary factor that precipitates it. It may also be of interest to study suitable appendices for viruses.

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Management Of The Immunized Obstetrical Patient

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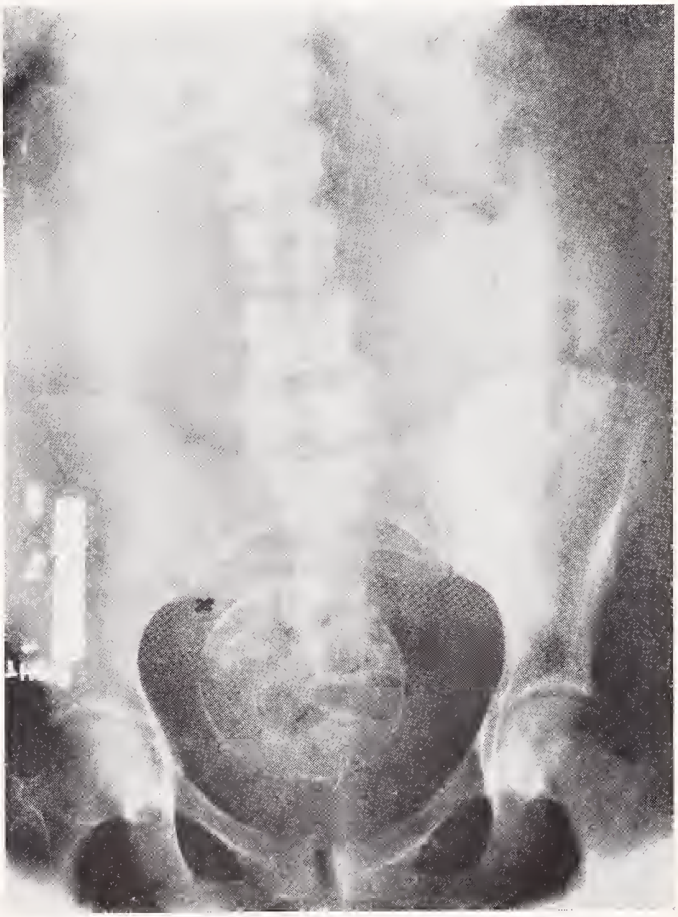
■ Erythroblastosis fetalis, or hemolytic disease of the newborn, is caused by an incompatibility of fetal and maternal blood. Maternal antibodies develop as a result of an immune response to an exposure to blood antigens, absent in the maternal circulation. This exposure may have been from a transfusion (or injection) of blood, or from the transplacental passage of fetal erythrocytes into the maternal circulation. The resultant antibodies may then cross back through the placenta and enter the fetal circulation. If the fetal erythrocytes contain the corresponding antigen, the maternal antibody may coat and destroy the fetal erythrocytes, hence the basis for hemolytic disease of the newborn.

Over the past few years increasing interest has been focused on this disease. Research in this area has brought about some changing concepts of management with a resultant lowering of perinatal mortality.

Amniocentesis

The most significant contribution to this field since the exchange transfusion has been the amniocentesis. In 1956, Bevis[1] showed that analysis of amniotic fluid in infants with erythroblastosis fetalis revealed increased blood pigments which are believed to be a reflection of increased erythrocyte destruction in the fetus. Walker,[2] Liley[3] and Mackay[4] subsequently reported impressive series relating the level of bilirubin content of the amniotic fluid (as measured by both chemical and spectrophotometric methods) to the severity of the disease in the infant. Some of the investigators have even recommended specific weeks of gestation for delivery based upon these amniotic fluid bilirubin determinations. The recommended time for amniocentesis is approximately 32 weeks of gestation. Several investigators recommend serial taps 2-3 weeks apart.[3,5]

If the fetus can be palpated readily, the technique of obtaining amniotic fluid is relatively simple at 32 weeks' gestation. The fetus generally lies in an attitude of flexion. The most favorable site of the tap is between the occiput and back of the infant as indicated in the photo by a black "x". The abdomen is prepared and draped in a sterile fashion. A 20 or 22 gauge spinal needle with a stylet is used. Infiltration with local anesthesia is generally not necessary. The operator stabilizes the fetal head with one hand, and passes the needle through the abdominal and uterine walls with the other. The stylet is removed and the needle is aspirated with a syringe. If correctly placed, 5-10 cc of amniotic fluid can readily be aspirated. If not, adjustment of depth will usually produce a free flow. In the event that no fluid can be aspirated, another tap in a different site may be attempted. The site recommended by Walker and Jennison[2] is on the side opposite the back in the area of least resistance to palpation which would represent the position of the flexed arms and legs. This generally is slightly below and lateral to the maternal umbilicus. This site is indicated in the photo by a white "x".



Abdominal flat plate at 32 weeks' gestation: The black "x" is the proposed site for amniocentesis described above. An alternate site described by Walker and Jennison[2] is marked by a white "x".

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Prior to the formation of vernix the amniotic fluid is clear. After vernix developes the fluid may be turbid. Normal amniotic fluid may vary from colorless to pale straw. When darker shades of yellow are encountered, there is a good correlation of intensity of yellow with the bilirubin content determined chemically and spectrophotometrically. The higher the bilirubin content, the more severely affected the fetus and the earlier the delivery should be. The amniocentesis, therefore, serves two useful purposes:

A. to indicate the normal or mildly affected infants who may be allowed to remain in utero in order to gain valuable maturity.

B. to indicate the more seriously affected infants for pre-term delivery in order to decrease the incidence of intra-uterine demise.

Antepartum Management

At the initial office visit, the obstetrician should take a careful history concerning injections of blood, blood transfusions and the outcome of previous pregnancies. A history suggesting erythroblastosis fetalis is of the utmost importance. Transcript of obstetrical experiences should be obtained from the former physicians.

The blood group and Rh must be determined on all new obstetrical patients. Wallet cards stating a patient's blood group and Rh factor should be viewed with skepticism unless the physician is familiar with the reporting laboratory. A blood group and Rh need not be repeated on subsequent pregnancies if the physician is confident that the data are correct. An indirect Coombs test, however, should be done early in each pregnancy to screen for maternal antibodies regardless of whether the mother is Rh-positive or Rh-negative. This test is valuable in that it may detect the presence of unsuspected antibodies (as Kell, C,c,D,E, or e). Once the laboratory has identified the maternal antibody, an antibody titre is indicated. This serves as a baseline for any subsequent titre determinations.

The next step is to obtain blood from the father. If his blood has the antigen corresponding to the maternal antibody, the set-up exists for erythroblastosis fetalis. The laboratory can be of further help in genotyping the father to determine if he is homozygous or heterzygous for this antigen. If he is homozygous, erythroblastosis fetalis should be anticipated; if he is heterozygous, the infant may or may not have the disease.

On the first office visit it is very important to establish the exact period of gestation. Since preterm delivery is the very basis for preventing intrauterine death, knowledge of the exact period of gestation becomes crucial. The date and character of the last menstrual period and any subsequent vaginal bleeding should be accurately noted. The size of the uterus in early pregnancy usually corresponds quite well to the period of gestation. An impression that the uterus is larger or smaller than expected should raise serious question as to the correctness of the duration of gestation. This may avoid the grave error of inducing labor, for example, at 33 weeks of gestation, believing the patient to be at 37 weeks of gestation.

There is no known medication that will safely prevent rise in antibody titre. There is no known medication that will improve the outcome of the infant. Steriods, antihistamines, desensitization and bioflavinoids have had adequate trials with no proven benefit. These should be avoided lest they offer the patient a false sense of security. The patient should be afforded general measures for good ante partum care, as prenatal vitamins, supplemental iron and daily rest.

At subsequent antepartum visits it is important to note the date of quickening and initial detection of the fetal heart and to estimate the gestational size of the uterus. These observations may corroborate that the expected date of confinement is indeed correct. Careful attention to the antibody titres is most important. These should be done on the initial visit, at 32, 36 and 38 weeks, gestation. More frequent titres are costly and rarely are of benefit. Careful attention should be paid to the clinical progress of the infant. The obstetrician should be watchful for signs indicating a poor prognisis. Hydramnios and a definite decrease in the activity of the fetus may be ominous signs when severe erythroblastosis fetalis is suspected.

Preterm delivery has markedly diminished the incidence of intra-uterine death and in some instances has increased the post natal survival. In the determination of the optimal time for preterm delivery, two factors which are of prime importance are serial antibody titres and amniotic fluid bilirubin content.

In the first immuized pregnancy (the first pregnancy during which antibodies are detected) the serial antibody titre is generally a good index of the severity of the erythroblastosis fetalis. A rapidly rising titre strongly suggests a severely affected infant. Amniotic fluid bilirubin determinations corroborate the clinical picture indicated by the antibody titre. In some instances there may be a rapidly rising titre indicating severe disease but the amniotic fluid bilirubin content will indicate that it is safe to allow the fetus to remain in-utero a short while longer, gaining precious maturity.

In *subsequent immunized pregnancies,* there may be a "residual" or "holdover" titre from the last pregnancy and this may fluctuate up or down irrespective of whether the blood of the fetus has corresponding antigen. The explanation for this is not clear. One patient beginning her pregnancy with an anti-D titre of 1:32 had a progressive antibody titre rise to 1:512 but the infant was found to be Rh-negative. In an instance like this, the titre may be totally misleading. It is in this subsequent immunized pregnancy that the amniocentesis has proven so valuable. The antibody titre may fluctuate up or down or even remain "fixed" at one level without reflecting what is going on in-utero. The amniocentesis, however, relates *only* to the *current* pregnancy. An amniocentesis done at 32 weeks' gestation may indicate if the fetus is undergoing rapid deterioration. If the fluid has a low bilirubin content, the obstetrician can be assured that the fetus will not die from erythroblastosis fetalis in the next few weeks. A follow-up tap done 2-3 weeks later will be helpful in determining any change in the in-utero status. It is not possible to predict definitely that the fetus is Rh-positive or Rh-negative but only that the fetus is not undergoing rapid deterioration. This procedure has greatly reduced the problem of intra-uterine death. It might be desirable to perform the amniocentesis at an earlier date than 32 weeks, for instance, if in previous pregnancies there had been an intra-uterine death at an earlier date of gestation. When the amniotic fluid is markedly bile stained, the fetus rarely survives more than a few weeks in-utero.

Delivery Of The Immunized Patient

Every major institution with good statistics for fetal outcome with erythroblastosis fetalis, attributes much of this success to interdepartmental cooperation. The obstetrician keeps the blood bank and the pediatrician informed of the existence of immunization problems and the projected time of delivery. It is best to have the pediatrician in the delivery room when the infant is delivered. Whenever possible the delivery should be accomplished in the daytime so that the blood bank and chemistry laboratory can operate at peak efficiency.

After the date of delivery is decided upon, the obstetrician chooses the mode of delivery. Needless to say, preterm delivery does not necessarily commit one to a Cesarean Section. Since the patient is usually parous, it is possible that induction of labor with an oxytocic agent can be accomplished with facility. Often the first day must be spent "softening" or "ripening" the cervix. The oxytocic may be stopped, and the patient allowed to rest over night. Induction of labor the following day generally is successful. Inductions of labor should be carried out under close medical supervision. Great care should be exercised to avoid a tumultuous labor. In certain instances the infant's condition is too compromised to risk a long induction. In such cases a Cesarean Section would be preferable.

The number of fetal erythrocytes circulating in the maternal blood stream has been shown to be markedly increased post-partum.[7] Implicated as a cause have been tumultuous labor, Cesarean Section, manual removal of placenta or any manipulative procedure at the time of delivery.[6,8,9,10]

The management of the third stage of labor plays an important role in the invasion of the maternal blood stream by fetal erythrocytes, possibly causing further immunization. Manual removal of the placenta has been shown to allow more than twice as many fetal erythrocytes to enter the uterine pool (the contents of the uterine cavity immediately following delivery of the placenta) than does spontaneous delivery of the pacenta.[10] Chromate tagged erythrocyte studies have demonstrated that the content of the uterine pool may enter the maternal circulation.[11] If possible, manual removal of placenta should be avoided in patients whenever there is an immunization hazard. As soon as the infant is delivered it is best to drain the residual blood from the placenta. This will obviate an elevation in pressure on the fetal side of the placental vascular system when the uterus contracts upon the placenta. This will allow fewer fetal erythrocytes to be available to the uterine pool. When the residual blood is drained from the cord the blood is saved for the appropriate laboratory studies (cord blood hemoglobin, bilirubin, Coombs test, etc.). When possible it is preferable to avoid the Trendelenberg position since this impedes good uterine drainage. Ergot-like ecbolics seem to be superior to oxytocin because they produce tetanic contractions of the uterus. Consequently there is less likelihood that blood in the uterine pool will enter the maternal circulation.[11]

Intra-Uterine Transfusion

In October, 1963, the first successful intra-uterine transfusion was reported.[12,13,14] A needle was passed into the amniotic cavity and bile-stained fluid aspirated. Then radio-opaque dye was injected into the amniotic cavity. After two hours the fetus had ingested the radio-opaque fluid. By this method the fetus and its gastrointestinal tract could be outlined on X-ray. Then a 16-gauge Tuohy needle was passed through the maternal abdominal wall, through the uterine wall and into the fetal peritoneal cavity. A polyethylene tube was threaded through the needle and the needle withdrawn. Approximately 100 cc of Rh-negative blood was then injected into the peritoneal cavity of the fetus. Approximately one-half of this was then absorbed into the fetal bloodstream from the peritoneal cavity. This was repeated again in ten days. The infant was delivered at 35 weeks and had a cord hemoglobin of 6 grams. Examination of the cord blood revealed that 50 per cent of the erythrocytes contained adult hemoglobin and were therefore traceable to the intra-uterine transfusions.

This procedure is indicated only when the fetus would die before it becomes mature enough for a preterm delivery. Our experience with the intra-uterine transfusion has been rewarding. Of the three infants salvaged by this procedure, one had a cord hemoglobin of 5.8 grams with 92 per cent adult (transfused) erythrocytes, another 6.2 grams with 70 per cent adult erythrocytes and a third with 6.7 grams with 65 per cent adult erythrocytes.

Maternal Hazard

Little emphasis has been paid in the literature to the maternal hazard of immunization in pregnancy. There is a risk of hemorrhage and transfusion in every obstetrical procedure. Depending on what specific antibodies are involved, the problem of finding a compatible supply of blood may be great. If a patient is immunized to a factor, the donor blood must lack that factor. If the patient is immunized to "c" or "e", it is very important to remember that this patient must not be given Rh-negative blood. The patient may be immunized to a combination of factors, making the finding of a compatible supply of blood extremely difficult. It has been suggested that plasmaphoresis be considered in this situation. The patient can then receive her own packed red blood cells, stored in the blood bank for transfusion, if the need arises.

Summary

The problem of iso-immunization is one of the most common and difficult complications of pregnancy. A logical and organized approach to the management of such patients should result in a diminution of perinatal mortality. A proposed outline of management has been presented.

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"I am an old man and death has robbed me of the dreams of youth—may those who do not know what old age means bear it with what patience they may when they reach it, because it cannot be imagined beforehand."

—Michael Angelo

The Immediate And Delayed Effects Of Acute Cerebral Anoxia

Gordon J. Gilbert, M.D.

From moment to moment the brain is remarkably dependent upon the integrity of its oxygen supply, as it utilizes some 20 to 25 per cent of the cardiac output and total body oxygen consumption. The effects of acute hypoxemia are usually sudden and dramatic, whatever their origin (be it failure of cardiac output or of pulmonary oxygen uptake, or disruption of the blood's oxygen-carrying capacity as in carbon monoxide poisoning). Cerebral neurons are particularly susceptible to anoxic damage, while astrocytes, oligodendrocytes, and microglia are much more resistant. Even among the cerebral neurons, certain populations demonstrate enhanced sensitivity to hypoxic deterioration. The neurons of the hippocampus are, for example, highly susceptible to hypoxic injury, and involvement of this medial temporal lobe structure appears responsible for the marked and persistent defect in recent memory which may follow an acute hypoxic episode. Bilateral surgical ablation of the hippocampus has been found to effect severe impairment in the ability to remember. The second and third layers of the cerebral cortex are also remarkably sensitive to hypoxia, and post-anoxic dementia probably relates particularly to cortical laminar necrosis. Similarly, hypoxic susceptibility of the basal ganglia, and particularly the globus pallidus, is reflected in the occurrence of a post-anoxic Parkinson's syndrome. Following acute carbon monoxide poisoning, the syndrome of typical Parkinsonian posture and rigidity can be correlated with the presence of bilateral cystic necrosis of the globus pallidus.

Involvement of the Purkinje cells and dentate nucleus of the cerebellum results in the signs of cerebellar dysfunction and probably in the myoclonic jerkings of the extremities which may persist long after an episode of moderately severe hypoxia. The myoclonus seen in these patients has a cerebellar quality and is activated by attempts at coordinated movement. There may be associated electroencephalographic abnormalities such as multiple spikes and spike-wave bursts. The occurrence of myoclonus as a sequel to brain hypoxia probably signifies a tendency in the individual for neurons generally to respond to mild disruption of their metabolic function by breakdown first in membrane ionic stabilization, resulting in seizure activity. At the cortical level, such neuronal hyperirritability may produce grand mal seizures, while when initiated at the level of the dentate nucleus, it may effect the sudden, involuntary jerks of myoclonus.

In recent years there has been increasing awareness of a syndrome of late deterioration in patients demonstrating initial recovery from a bout of severe cerebral anoxia. The patient usually awakens within 24 hours following the acute anoxic episode, and may become fully active within four or six days. After a lucid interval of from several days to several weeks, there is a recurrence of progressively worsening symptomatology including irritability, apathy, clumsiness, spasticity or rigidity, and confusion, progressing even to coma and death. Although the lucid interval might suggest the presence of subdural hematoma, detailed clinical and pathological evaluation has disclosed neither this nor any other known causes of coma. Post mortem examination in these instances has found, in addition to gray matter injuries consistent with the original, anoxic insult, a diffuse demyelination of the cerebral central white matter, though with "arcuate sparing" of the white matter bordering the cortex. Numerous fat-filled macrophages signify the breakdown of myelin, and there is a moderate proliferation of astrocytes, the "scar cells" of the central nervous system. Remarkably, the oligodendrocytes remain apparently intact. Modern understanding of cerebral myelin and the demyelinating diseases has focused attention upon the critical importance of the oligodendrocytes. Myelin is apparently formed by the oligodendrocyte's wrapping its own cell membrane repeatedly about the axon, creating a vortex arrangement having the axon at its center, and the body of the oligodendrocyte at the periphery. Thus, in the condition of delayed post-anoxic deterioration, the intact morphology of the oligodendroglia, despite the marked disruption of myelin, might at first glance appear quite remarkable. Another factor, however, is known to be of great importance in the maintenance of myelin; if the axon of a peripheral nerve is cut away from its cell body, not only will the axon die, but the myelin distal to the cut will also degenerate. In the central nervous system, too, myelin viability is exquisitely

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dependent upon axonal integrity, and normal myelin has never been described in the absence of a central axon. Since the axon is, in turn, quite dependent metabolically upon the neuronal cell body, a moderate deficiency in the availability of cell energy might well be reflected at the distal, axonal level, with a loss of whatever it is the axon contributes to maintain its myelin coating. The intense disruption of myelin which appears to underlie late post-anoxic deterioration, may then, be yet another reflection of anoxic gray matter disease of such severity as to produce metabolic disruption at the axonal level but not necessarily sufficient to alter the neuron histologically. Axonal insufficiency need not be associated with histologically apparent cell body alterations, as diminished production at the cell body may be manifested first where the lines of supply are longest. The onset of myoclonus and hallucinations during late post-anoxic deterioration strengthens the suggestion that disease of the gray matter plays a fundamental role, since both hallucinations and myoclonus are regarded to be manifestations of neuronal hyperirritability as may be seen in mild or moderate neuronal energy deficiency states. The axon's central importance in myelin *maintenance* has received little attention by students of demyelinating disease, and instead, interest has focused upon the oligodendrocyte and its role in myelin *formation.* It may be significant, however, that in many of the "demyelinating" diseases the pathological disturbance is a *breakdown* of myelin and its engulfment by macrophages, rather than a gradual disappearance of myelin as might be expected were demyelination simply a matter of metabolism's exceeding a reduced anabolic capacity.

Four other hypotheses have been proposed to explain late post-anoxic deterioration associated with central demyelination. Some authors have suggested that the late demyelination is of vascular origin; the initial episode of anoxia would so damage blood vessels of the central white matter that their subsequent deterioration would lead to the observed demyelination. However, recent observations at autopsy[3] have disclosed no vascular disorder whatsoever. Another hypothesis has held that cerebral edema, known to follow brain injuries of diverse sorts, becomes particularly intense in the central white matter of these patients and is responsible for the observed disruption of myelin. However, while edema is generally maximal by the second to fourth day after injury, late post-anoxic deterioration may begin as late as two or three weeks after the anoxic episode. Furthermore, signs of increased intracranial pressure, as might be expected in patients suffering severe edema of the central white matter, have not been seen in these patients.

A third hypothesis held that the initial brain damage caused by anoxia might have triggered the occurrence of an allergic encephalomyelitis. The timing of the late deterioration is certainly consonant with such an hypothesis; however, once again the pathological picture fails to support the hypothesis, and there is no evidence of the perivenous accumulations of lymphocytes or perivascular foci of demyelination so characteristic of allergic encephalomyelitis.

Plum and associates recently proposed that the late disruption of myelin is caused by a failure in myelin synthesis by oligodendrocytes damaged in the acute hypoxic episode, the delayed onset of demyelination then relating to the normally slow turnover of myelin. However, the resistance of the glia to anoxia considerably exceeds that of the cerebral neuron, while the intact morphology of the oligodendrocytes certainly fails to support this hypothesis. Also, each oligodendrocyte covers only a small segment of a central axon, just as a Schwann cell covers only an internode of a single peripheral axon. In peripheral nerve demyelination caused by Schwann cell disease (as in diphtheritic neuritis), what is seen is a "segmental demyelination," small segments of myelin, (corresponding to single Schwann cells) dropping out in scattered fashion. A similar situation might be expected in the central white matter were demyelination of an oligodendrocytic origin. A segmental type of demyelination is indeed seen centrally in multiple sclerosis, a disease characterized by *focal* areas of demyelination which might well relate to focal disruption of oligodendrocytic activity. However, the *diffuse* central demyelination seen in the late-deteriorating anoxic cases is not of this nature, and would seem more consistent with the axonal insufficiency hypothesis. There is evidence[3] that these patients may have been permitted to resume vigorous mental and physical activities too soon after the anoxic attack. On both theoretical and practical grounds, the treatment of a patient who has suffered an episode of acute cerebral hypoxia should include a lengthy period of complete physical and mental rest, as well as optimal oxygenation and nutrition.

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Clinical Medicine

Hyperbaric Oxygenation

David M. Little, Jr., M.D.

■ The news that one of the major hospitals in Connecticut is considering the construction of a hyperbaric chamber brings to mind the statement by Sir Michael Foster that science travels in circles —the concept that was followed yesterday may be dropped today and rediscovered tomorrow. This has most certainly been true of hyperbaric therapy as a clinical tool in medicine. More than a century ago a number of health spas in Europe offered hyperbaric therapy for a variety of ills; and Paul Bert's classic volume on the physiological effects of barometric pressure, which was published in 1878, describes a number of these facilities and therapeutic endeavours.[1] In time, however, it became obvious that many of the claims made for hyperbaric therapy by its proponents (and the spa owners) could not be substantiated, and the method gradually fell into disuse and was abandoned. Less than a decade ago, however, a serious reinvestigation of hyperbaric oxygen therapy was undertaken by Boerema in Amsterdam,[2] and shortly thereafter by Sir Charles Illingworth and his department at Glasgow.[3] Enthusiastic interest spread across the ocean about two years ago, and today hyperbaric chambers are being constructed or planned for construction at a number of centers in this country.

The greater part of the oxygen transported by the blood under the normal circumstances of one atmosphere of pressure is carried in the red blood cells combined as oxyhemoglobin. In a patient with normal hemoglobin level, breathing air at normal atmospheric pressure, arterial blood contains about 19.5 volumes of oxyhemoglobin per 100 cc. of blood. At this level the hemoglobin is about 95 per cent saturated, so there is very little scope for improvement. However, oxygen is also carried in the blood in simple physical solution in the plasma. Under normal conditions of atmospheric pressure only a very small amount is carried this way—approximately 0.25 volumes per cent—but this is of special importance because, since it is a physical solution, its level can be raised simply by raising the ambient pressure. In the case of the human subject, it is necessary to place the patient in a pressure chamber and administer oxygen. When this is done, and the pressure is raised to two atmospheres (absolute), the amount of oxygen in solution in the plasma is raised from 0.25 to 4.2 volumes per cent—this is to say, more than sixteen times the normal level. The total effect of this is to raise the oxygen content of the blood from rather less than 20 volumes per cent almost up to 25 volumes per cent—a quite considerable increase. Furthermore, in addition to this there is a further potential benefit, for by increasing the tension of oxygen in the blood-stream the rate of diffusion into under-perfused and anoxic tissues is enhanced. For while the red cells act as floating store houses of oxygen, the rate at which oxygen will diffuse from the blood, through the capillary wall, to the tissue fluids, and hence to the fixed cells of the part, depends upon the gradient of partial pressures between the plasma and the tissue cells.

These facts have allowed the Dutch group to dilute the circulating blood of the pig, using plasma and macrodex to replace the removed whole blood, until only 0.4 per cent of the original hemoglobin remained.[4] The blood at this dilution was a clear liquid and the animals were of a startlingly pale color, but in oxygen under three atmospheres of pressure they maintained normal electrocardiograms throughout the experiment. On the contrary, under 100 per cent oxygen but at normal atmospheric pressure, the hemoglobin could be reduced only to 11 or 12 per cent before abnormalities were observed on the electrocardiogram.

This ability of hyperbaric oxygenation to saturate the whole body, the blood plasma, the intercellular fluid, and the cells themselves, with a very high level of physically dissolved oxygen originally led to its present-day reinvestigation as an aid to open-heart surgery, but it soon proved to be of value in other fields.

As might be anticipated, drenching the body with oxygen has been particularly beneficial in the treatment of anerobic infections. In the therapy of Clostridium Welchii infections, hyperbaric oxygenation has resulted in detoxication within 24 hours, and has permitted postponement of radical amputations and the subsequent sparing of many extremities. Antibiotics have been administered against secondary infections, but the use of anti-

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gas-gangrene serum has not been necessary. Of 26 patients treated in the Surgical University Clinic in Amsterdam, in only one patient was death clearly due to gas gangrene, and in one other patient the cause of death was indirectly related to the infection.[5]

In carbon monoxide poisoning, hyperbaric oxygenation at two atmospheres of pressure has been shown to be far more effective than either 5 per cent or 7 per cent Carbogen mixtures or 100 per cent oxygen at ambient pressure. This form of treatment rapidly corrected the anoxia and increased the speed at which carbon monoxide was removed from the blood and tissues. Of 22 patients with severe carbon monoxide poisoning admitted directly to the Western Infirmary in Glasgow during a recent 12-month period, all recovered completely despite the fact that the carboxyhemoglobin content averaged 40 per cent, and ranged as high as 69 per cent, on admission.[6]

Hyperbaric oxygenation has been employed rather extensively in the treatment of peripheral vascular insufficiencies. Acute arterial insufficiency, caused by injury to the main vessels to a limb, has been treated in the hyperbaric chamber with promising results, the immediate danger of gangrene being averted until sufficient collateral circulation could develop to maintain the vitality of all or most of the part. Chronic arterial insufficiency and soft tissue necrosis have shown improvement in healing ability in situations not amenable to correction by surgery. Patients with chronic obliterative disease of the lower extremity, such as atherosclerosis or thromboangiitis obliterans, do not, of course, show improvement of the gross organic vascular changes, but in many such patients the severe rest-pain—often severe enough to prevent sleep—was relieved.[7]

The initial research studies and clinical experiences from the group in Glasgow indicate a possible potential in the treatment of extensive myocardial infarction. They ligated the main left coronary circumflex artery in the dog, and were able to reduce the mortality rate from around 50-60 per cent in unprotected dogs down to 10 per cent in animals breathing oxygen at 2 atmospheres of pressure. The therapy has been applied to human beings for periods up to 3½ days with complete recovery and no evidence of subsequent hemodynamic failure.[8]

The Glasgow group also has investigated the effect of hyperbaric oxygenation on cerebral vascular occlusion in the dog by occluding both carotid and both vertebral arteries low in the neck. When this was done at atmospheric pressure, signs of cerebral anoxia developed rapidly, the electroencephalogram showing deterioration within 15 seconds and a complete loss of cortical rhythm within 1 minute. By contrast, when the clamps were re-applied during full oxygenation at two atmospheres of pressure, the electroencephalographic record remained normal throughout the experimental period of about 30 minutes.[7] These observations could have important clinical implications in relation to cerebrovascular disease and in relation to operations on the brain.

Its potential value in open-heart surgery, as already mentioned, underlies much of the recent interest in hyperbaric oxygenation. As an adjunct in major surgery for patients with increased cardiac risk it is of proven value, for the patient's state of oxygenation can be improved immensely before surgery. Reduction of cardiac irritability and the prevention of ventricular fibrillation has been demonstrated by Boerema's group; and they have been operating on deeply cyanotic children with congenital heart disease who would have been inoperable otherwise.[9]

The most longstanding of the newer applications of hyperbaric oxygenation has been its use as an adjunct to radiation in the treatment of malignant tumors. Hypoxia reduces the sensitivity of tumor cells to radiation, and many viable tumor cells are probably rendered hypoxic because of inadequate blood supply. In the past, attempts have been made to return anoxic tumor cells to full radio-sensitivity by the inhalation of oxygen at atmospheric pressure. Hyperbaric chambers are now being utilized as a means of increasing the oxygen tension in tumors and thus increasing the radio-sensitivity of the tumors.[10]

The therapeutic applications of hyperbaric oxygenation thus are impressive and provide apparent justification for the current enthusiasm, but there are a number of problems that must be solved before widespread use is feasible. The facilities needed in such therapy—that is to say, the hyperbaric chambers themselves — are large, complex, expensive and potentially dangerous. They must be designed and installed under the most exacting codes, with adequate safeguards against explosion, fire, accidental decompression, toxic fumes, and so forth. Furthermore, a number of human hazards, to both patients and medical personnel, are encountered under hyperbaric conditions, especially when oxygen is introduced. While the most serious of these is oxygen toxicity, there is also danger of arterial gas embolism, decompression sickness ("the bends"), and minor pressure problems relating to gas-filled spaces including the paranasal sinuses, the middle ear, gas-containing periapical tooth abscesses, and the large bowel. The paramount consideration that must be determined, however, is whether hyperbaric oxygenation will be uniquely beneficial and fully practical in its use in at least a few important conditions in a reasonable number of patients. The occasional use of a hyperbaric chamber for anaerobic infections, carbon monoxide poisoning, scuba accidents and the like would hardly justify the difficulties, possible dangers, time and expense involved in the installation and maintenance of such chambers; but the possible potential, if proven, in such common conditions as coronary occlusion, cerebrovascular disease, shock, and certain operations could make hyperbaric oxygenation a most important addition to the therapeutic armanentarium.

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Poor P.B.I. And Iatrogenic Hypothyroidism

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■ All physicians are acquainted with the limitations in measuring the basal metabolic rate, (B.M.R.), accurately in patients. Lack of proper preparation, irregularities of breathing pattern, poor fit of the mouth-piece, fever, anemia, dyspnea, and anxiety all contribute to the inaccuracy of the method. It is not well known that some euthyroid patients may have values 20 per cent or more below standard without objective evidence of hypothyroidism by use of other thyroid function tests.

For these reasons as well as for the convenience of the patient, the protein bound iodine (PBI) and its modifications, the butanol extractable iodine (BEI) and the thyroxine iodine (T4), has supplanted the BMR.

The limitations of the PBI test and its modifications are not as well known. The PBI may be falsely elevated by ingestion of inorganic iodides, some apparent such as potassium iodide, Lugol's solution and some not so apparent as minerals added to therapeutic vitamins and the iodine compounds of organic drugs (Ornade, Combid, Darbid, etc.). The T4 and BEI modifications of the PBI method will measure accurately the serum thyroxine in these instances of inorganic iodide contamination of the serum. The PBI may also be elevated early in the course of infectious hepatitis and in acute thyroiditis. BEI and T4 levels may be normal in hepatitis but in thyroiditis, a discrepancy between an elevated PBI and low or normal BEI or T4 is often recorded and is helpful in establishing this diagnosis.

The PBI, BEI, and T4 may be falsely elevated by recent administration of organic iodine dyes used in cholecystography, pyelography, angiography, and myelography. With one particular gall bladder dye, Teridax, not used widely at present, elevations of the PBI, BEI and T4 may last as long as 33 years after ingestion. The PBI, BEI and T4 may also be elevated in pregnancy and by estrogen and anovulatory drugs (Enovid, etc.), because the total concentration of thyroid binding globulin in the blood is increased. There have also been rare euthyroid families reported who have a familial increase in thyroid binding globulin and therefore elevated PBI, BEI and T4 levels.

Injections of mercurial diuretics falsely lower PBI, BEI and T4 levels if the acid ash method is used because the iodine is precipitated by mercury during digestion. The effect may last as long as 72 hours but is usually over in 24 hours. Ingestion of Dilantin lowers PBI, BEI and T4 levels by displacing thyroxine from thyroxine binding globulin. It has no effect on thyroid function. Ingestion of triiodothyronine (Cytomel) may lower the PBI, BEI, T4 levels in euthyroid patients because it sup-

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DR. WILLIAM F. ECKHARDT, JR., is Attending Physician, The Stamford Hospital, Stamford. Associate Physician, The Norwalk Hospital, Norwalk.

presses thyroid thyroxine production and is not measured because it is loosely bound to thyroid binding globulin and is not precipitated during the chemical determination.

In the management of hypothyroidism, most physicians use the PBI or its modifications, (BEI or T4), to follow the effect of replacement thyroid medication. Most of the time the PBI shows an appropriate rise to euthyroid levels on adequate dosage of thyroid extract. There have been problems in gauging adequate replacement levels in some patients. Lavietes and Epstein reported on the course of 15 patients with unequivocal untreated hypothyroidism.[1] The PBI level in their patients varied greatly when they were placed on equivalent amounts of thyroid extract, thyroglobulin (Proloid), synthetic thyroxine (Synthroid) and triiodothyronine (Cytomel). Although the patients remained Euthyroid, the PBI values observed were almost zero with triiodothyronine, subnormal with thyroglobulin, low to low-normal with thyroid extract and high to hyperthyroid with synthetic thyroxine. Braverman and Ingbar have also reported that thyroglobulin (Proloid) was observed to decrease the PBI of euthyroid patients, often into the hypothyroid range, and failed to increase the low PBI significantly of hypothyroid patients.[2]

Nine patients have been personally observed who displayed the paradox of diminishing PBI levels in the hypothyroid range while taking increasing amounts of thyroid extract or thyroglobulin. Two patients clinically hyperthyroid had PBI levels under 1.5 micrograms per cent and 24 hour thyroidal radioactive iodine uptakes under 5 per cent while taking 5 grains of thyroglobulin daily. Both patients responded normally to injections of thyroid stimulating hormone by a rise in the radioactive iodine uptake to normal values. When the patients were changed to equivalent dosages of synthetic thyroxine, a rise in the PBI from 1.3 to 7.5 micrograms per cent was observed. When all thyroxine medication was discontinued for six weeks, the PBI and T4 levels became and remained normal. Of the nine patients seen, only two had true hypothyroidism. The euthyroid patients had been given thyroid extract as a tonic, an aid in the correction of menstrual irregularities; an aid in weight regulation or as treatment of psychiatric depressive reactions.

The reason for the failure of the PBI, BEI and T4 to accurately reflect the clinical status of patients receiving thyroid extract or thyroglobulin as replacement is, that these materials contain an unknown amount of triiodothyronine which has a biological effect but is not measured in the PBI. The ratio of triiodothyronine to thyroxine in thyroid extract from different species and in different lots may vary from 2:1 to 3:1.[3] Thyroid extract seems to deteriorate with age and it is difficult to determine the potency of thyroid tablets kept for an unknown period on the pharmacist's shelf and in the patient's bath-room cabinet. The USP assay for potency of thyroid extract is based on total iodine content which assumes a quantitative relationship between biologically active iodine and total iodine. Recent pharmacological studies have cast doubt on the validity of this assumption.[3] Some forms of thyroid extract, mostly from European suppliers, have been found to be sub-standard or lacking in metabolic effect even if they meet the USP assay standards.

Synthetic thyroxine requires no assay to insure potency. Its major disadvantage seems to be a philosophical one that it may not be equivalent to the balance of triiodothyronine and thyroxine supposedly secreted by the normal thyroid gland. Evidence for this view is lacking since hypothyroid patients when made euthyroid, fail to note any differences between synthetic thyroxine and active thyroid extract.

This observer favors the use of synthetic thyroxine since no patients have shown the paradox of diminishing PBI concentrations on long-term dosage. It must always be remembered that PBI levels in thyroxine treated patients will be on the high normal or occasionally low hyperthyroid level.

From the amount of thyroid extract sold and taken by patients, hypothyroidism must be an extremely common disease. Yet if patients are carefully studied, few satisfy the criteria for true hypothyroidism. All too many patients receive thyroid extract for treatment of fatigue and other nonspecific depressive symptoms. All too many patients receive thyroid extract to "treat" BMR levels that may be in the euthyroid range (+ 10 to − 20%) or PBI levels in the "low-normal" range, 4-5 micrograms per cent. There is a strong placebo effect created by an enthusiastic physician and "anti-fatigue" medicine.

A plea is made that objective testing be done before a patient is started on life-time thyroid replacement. Where a valid reason is found for thyroid replacement, all physicians must be aware of the limitations of the methods used in the initial testing and the effects of the thyroid material they use on the tests that are performed to gauge the improvement of the patient.

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2. Braverman, New England J. Med. 270: 439-442, 1964.

3. Devlin, W. F. and Stephenson, N. R.: The chemical determination of lithyronine and thyroxine in enzymic hydrolysates of pork thyroid. J. Pharm. & Pharmacol. 14: 597-604, 1962.

FROM THE GENERAL MANAGER'S OFFICE

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Assistant to General Manager

CALL
SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1964 Semi-Annual Meeting of the House of Delegates will be held at the Stratfield Motor Inn, Downtown, Bridgeport, commencing at 2:00 o'clock in the afternoon of Wednesday, December 9th.

Ralph L. Gilman, President
Kenneth F. Brandon, Speaker of the House
Denis S. O'Connor, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENT TO THE BYLAWS

The following proposed amendment to the Bylaws was presented to the House of Delegates on April 28, 1964 and was tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, this amendment will be published in Connecticut Medicine "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

Introduced by Jachin B. Davis, New Haven

ARTICLE X — COMMITTEES OF THE COUNCIL — Section 2 be amended as follows:

Par. 1. Delete line 9, "A Liaison Committee with CMS"

Par. 9. Delete entire paragraph which outlines duties of this committee.

NOTICE
COMMITTEE SERVICE QUESTIONNAIRE—THIS ISSUE

Each year the Councilors from the eight constituent county medical associations assume the responsibility of selecting members of the Society to participate in the various programs of the Society which are carried on through the activities of committees and related groups. In making these selections, it is of importance to choose physicians who are not only willing and able to serve but also who are known to have an interest in the work of committees and groups to which they may be assigned.

In 1961, a "Committee Service Questionnaire" was mailed to all members as a supplement to Connecticut Medicine and from the returns this office was able to furnish the Councilors with a compilation of those who had a desire to be nominated for committee service. In order to update this compilation, a second mailing of the questionnaire is made as a supplement to this issue of the Journal. Members are urged to indicate on the questionnaire their areas of special interest, and to return the completed form to 160 St. Ronan Street, New Haven.

NEW MEMBERS

Fairfield County

Arthur Brovender, Norwalk
Alan T. Cahill, Fairfield
James R. Dorr, Darien
Marshall Franklin, Norwalk
Russell A. Keddy, Stamford
Harry R. Kormos, Westport
Samuel H. Levy, Stratford
Lawrence G. Methot, Bridgeport
Arthur H. Michael, Bridgeport
Hyman Nadel, Glenbrook
Carlos Peralta, Bridgeport
John H. Prunier, Greenwich
L. Robert Rubin, Danbury
Gerard A. Sava, Stamford
James F. Silverman, Newtown
David P. Stiff, Bridgeport
Richard L. Van de Berghe, Fairfield

Hartford County

Charles W. Avery, Hartford
Stanislaus A. Bartus, Hartford
Paul Clapp, New Britain
James C. Collias, New Britain
John J. Davenport, Jr., Hartford
Brendan M. Fox, Hartford
Ralph M. Gofstein, New Britain
William A. Gryboski, New Britain
Jay M. Hughes, Manchester
Joseph R. Jurkoic, New Britain
James G. Katis, Hartford
Thomas P. Kugelman, Hartford
James M. Labraico, Bristol
Robert Livingston, West Hartford
Joseph R. Lusby, New Britain
Iain M. Mackay, Hartford
Andrew A. Mayer, Hartford
John D. McCarthy, Hartford
Sidney Perlman, Hartford
Brooks, J. Poley, Hartford
Arnold S. Ritvo, Hartford
Richard W. Roberts, New Britain
Howard F. Root, Jr., New Britain
Robert S. Rosson, Hartford
Benjamin H. Schatman, Hartford
Walter T. Scudder, Simsbury.
Henry J. Sharon, Southington
Joseph B. Shaw, Manchester
George V. Smith, Hartford
Jay D. Smith, West Hartford
Theodore N. Smith, Hartford
Robert Wehr, Hartford
James M. Wilson, New Britain

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1964 MEETINGS

November 29-December 2—American Medical Association Clinical Convention, Hotel Americana, Miami Beach, Florida.

December 9—Semi-Annual Meeting of House of Delegates, Connecticut State Medical Society to be held at Stratfield Motor Inn, Bridgeport, Connecticut.

1965 MEETINGS

April 27-29—Connecticut State Medical Society Annual Meeting to be held at Statler-Hilton Hotel, Hartford, Connecticut.

PLACEMENT WANTED

GENERAL SURGEON—with experience in orthopedics, gynecology and urology interested in locating in Connecticut. Would prefer an association or group practice. 33 years of age and a Diplomate of National Boards.

G.P. and General Surgeon wishes to locate in southern Connecticut. either solo or group practice.

PLACEMENT OPPORTUNITIES

Litchfield County — Pediatrician and orthopedist wanted in Winsted, Connecticut area. This area is served by a small hospital and provides excellent opportunities.

Occupational physician wanted for state employee's clinic, located in Hartford. 35 hour week, 3 weeks vacation, up to 120 days sick leave, paid insurance program, social security and liberal retirement. Requires at least two years' general practice. Starting salary $11,640 going to $12,380 at end of year, then advancing $540 annually to maximum of $15,080. Reply directly to B. Dearington, State Department of Health, State Office Building, Hartford, Connecticut.

Opportunity for Board eligible or Board qualified Pediatrician, Orthopedist and Radiologist to associate with group of young specialists in newly constructed building to be completed July, 1965. New Haven Hospitals close by.

ANY PERSONS INTERESTED IN THE ABOVE ARE ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN.

REPORT OF THE MEETING OF THE AMA COMMITTEE ON OSTEOPATHY AND MEDICINE IN SAN FRANCISCO

June 21, 1964

Oliver B. McGilliendy, M.D., President-Elect of Michigan State Medical Society, presented a factual report on the Osteopathic Situation in Michigan. He stated that 20 per cent of the practicing physicians of Michigan are osteopaths (1,825 of 8,000). 258 of them are listed by their association as specialists. There are 38 osteopathic hospitals with 3,600 beds; there are 182 hospitals with 26,407 beds which limit their staff appointments to MD's. There are 13 hospitals (with 1,137 beds) which have joint MD-DO staffs.

Lansing, Michigan (the State Capital) has been chosen by the DO organization as the site for the projected 35 million dolar osteopathic medical school. The Chambers of Commerce of six other Michigan cities eagerly sought for the site for this projected Osteopathic Medical School probably because it promised the community 2,000 jobs. In Lansing 90 per cent of the DO's are members of the Chamber of Commerce, although less than 10 per cent of the MD's are dues paying members. Although the Michigan State University is starting a two year medical school in East Lansing, this did not deter the osteopaths who were commended by the State Legislature for their plan to build a medical school without State funds.

In some rural areas of Michigan the MD's and DO's are congenial and cooperative in their joint staffed hospitals. In most of the cities of 75,000 to 200,000 where the DO's have their own hospitals there is practically no fraternizing. However, after bitter controversy in four new community hospitals in the area south of Detroit, the osteopaths have won the first legal battle as to the staffing of these hospitals.

Both the University of Michigan Medical School and the Wayne University Medical School have welcomed osteopaths to their Post Graduate courses for several years. For the past three years the Wayne County Medical Society and the Michigan State Medical Society have had liaison committees for contact with the osteopathic association. There have been many meetings and many points of agreement but recriminations by the DO's in regard to the efforts of MD's to keep them from the staffs of the new community hospitals is the basis for most of their complaints. The osteopaths have avoided all efforts to discuss future amalgamation with the MD's. They recently rejected an offer by the Blue Shield of Michigan to seat one of their members on its Board of Trustees stating they would have four osteopaths on the Board or none. 619 osteopaths participated in Blue Shield last year and were paid 14 million dollars.

Many of their hospitals have passed recent inspections with high honors. It is rumored that DO's pay their hospitals a per diem sum for each patient admitted. The Lansing General Osteopathic Hospital was built by a community drive shared by two MD hospitals and had no difficulty borrowing a million dollars for expansion.

The Michigan State Medical Society Liaison with Osteopaths Committee passed a motion that county medical societies might invite selected osteopaths to their scientific meetings. They also moved that the State Society invite osteopaths practicing scientific medicine to State Post Graduate sessions and that the State Society continue to work toward a single Standard Medical Practice Act.

The Michigan State Board of Registration in Medicine has ruled that only members of the June 1962 or later graduating classes of the California College of Medicine can be considered for licensure.

A Policy Statement by Robert F. Benson, D.O., President of the Osteopathic Association of Michigan is as follows: "The Osteopathic profession has not sought amalgamation with the allopathic profession, it is not seeking it now and will not seek it in the future. We believe that the American Public would not gain by such amalgamation."

California

Doctor Samuel R. Sherman, Immediate Past-President of the California Medical Association, reported on the amalgamation of California. He stated that the merger was a success. He indicated that by the end of the next fiscal year, the members of the Forty-First Medical Society (former osteopaths) will all become members of the various regular county medical societies. Doctor Sherman pointed out that there was a problem relative to obtaining certification for former osteopaths. At the present time, the specialty boards will not recognize the former osteopaths who were certified. Accordingly, the California Medical Association has created its own Certification Review Committee to work on this problem.

A summary prepared by the Committee on Osteopathy and Medicine of the AMA has added considerable interesting data to the status of the merger in California. There have not been any complaints from former osteopaths that they have been financially hurt by the merger. In fact, some of them have gained financially since they are now receiving referals from both former DO's and MD.s' At the recommendation of the California Medical Society the California Hospital Association urged its member hospitals to change their rules so that membership in a component medical society (such as the 41st) rather than membership in the local medical society be one of the criteria for membership on a hospital staff. This was done and accordingly these members of the 41st Medical Society were qualified to make application for staff privileges in MD hospitals.

Some of the former osteopaths have been accepted as specialists in publicly owned MD Hospitals and a few have been taken on the staff of privately owned MD hospitals. The former osteopaths have been accepted as GP's in all of the private and public hospitals.

Following the merger, 65 DO hospitals became members of the California Hospital Association and the American Hospital Association. Some have been accredited by the Joint Commission on Accreditation of Hospitals while others have applied for this accreditation. The accreditation of the former DO hospitals have been accomplished with the same men, former osteopaths, heading the various services in the hospital.

There have been some changes in the California College of Medicine (formerly the Osteopathic College.) This college which accepts 96 students per year used to get applications from about 250 students. Last fall as an MD school it received 632 applications and already has received 855 applications for next year. This college now receives more applications than the Medical School of Stanford. Dr. Warren C. Bostick is the new Dean of the School as approved by the former osteopaths who negotiated the merger. The various department heads of the College are being replaced by MD's. This was considered to be in the best interest of the college and must be so if the residency and intern programs are to be approved. A number of former osteopaths who headed various departments have become senior attending physicians in the teaching programs of the college. Only one hospital, The Los Angeles County Hospital, has obtained approved residencies—one in internal medicine and the other in orthopedic surgery. There is, however, no need for former osteopathic hospitals to have intern and residency programs in as much as the graduates of the college may now go into programs in any of the MD hospitals of the county.

There are two law suits stemming from the merger. Both were by osteopaths who do not approve of the merger.

New York

James M. Blake, M.D. of Schenectady, New York, reported on MD-DO relations in New York. He stated that voluntary association of an MD with a DO is permitted providing the DO practices scientific medicine. He acknowledged that some DO's and MD's in New York have been consulting with one another.

Doctor Blake reported that some of the DO's who had received MD degrees from the California College of Medicine were seeking membership in various county medical societies and also in the state medical society. He stated that the state medical society voted not to accept these individuals into membership.

The committee on Osteopathy and Medicine of the AMA reported that approximately 15 osteopaths who obtained MD degrees from the California College of Medicine have had the letters MD inscribed on their licenses after the letters DO. Dr. Henry Fineberg of the New York Medical Socity has written to the Chancellor of the Board of Regents of the State of New York requesting that the Board review and reverse the ruling permitting osteopaths who have obtained a degree from the California College of Medicine to have the letters MD added to their license. The Board has not acted on this matter to date.

Washington

Dean K. Crystal, M.D., Immediate Past-President of the Washington State Medical Association, reported on recent developments of the proposed merger in Washington.

He stated that in 1962 the Washington State Medical Association voted to amalgamate with those DO's who were practicing scientific medicine. As a result, the Washington College of Physicians and Surgeons was created for the purpose of granting MD degrees to Washington DO's. Fifty-four osteopaths enrolled in the College and successfully completed a twelve-week course. While these individuals have earned their MD degrees, the College has been enjoined from issuing them their diplomas. In addition, on March 21, 1964, the Washington State Board of Medical Examiners voted three to two against granting MD licenses to the graduates of this College.

However, despite this setback, the proponents of amalgamation are optimistic concerning their program. A lawsuit in behalf of the American Osteopathic Association and the Washington Osteopathic Association has been filed against the Washington State Medical Association, the King County Medical Society and the King County Medical Service Corporation (Blue Shield) seeking 3 million dollars in damages on a new state anti-trust law and a conspiracy to destroy "osteopathy."

Missouri

Leonard T. Furlow, M.D., President, Missouri State Medical Association, reported on MD-DO relations in Missouri. He stated that the Missouri State Medical Association was very much interested in up-grading the osteopaths' education in Missouri. He indicated that his association was not interested in amalgamating the two professions.

According to the Committee on Osteopathy and Medicine of the AMA, the DO's are more opposed to the merger than the MD's. There are 1,116 osteopaths in Missouri and two DO schools. These schools graduate about 170 students each year. There is a composite licensing board consisting of 5 MD's and two DO's. The DO's are granted an unlimited license. Some time ago, as a result of a lawsuit, the DO's obtained staff privileges in public hospitals. Some hospitals have single staffs, others have dual staffs. There are 18 DO hospitals in Missouri.

Illinois

According to the Committee on Osteopaths and Medicine of the AMA representatives of the State Osteopathic Association met with representatives of the Illinois Medical Society seeking:

1. The right to participate in postgraduate medical education programs.
2. To consult with MD's and to be permitted to visit their patients in MD hospitals.
3. To participate in public health projects such as school examinations.

The osteopathic representatives refused to discuss converting the Chicago College of Osteopathy into an MD school. They were not interested in a merger of the two professions. Although the Illinois Medical Society disbanded its committee on osteopathy at the suggestion of the AMA committee it reactivated it to study osteopathic relations.

Iowa

At the request of the osteopaths and MD/DO Liaison Committee has been set up consisting of 5 DO's and 5 MD's. As a result of the activity of this committee a bill was passed by the Iowa legislature creating a composite board which is made up of 6 MD's and 2 DO's. The MD's and DO's take the same examination.

The College of Osteopathic Medicine and Surgery in Des Moines wishes to build a new 26 million dollar school and a 400 bed hospital on land given to the College by the Federal Government. Presently the College takes in 70 students a year; with its new facilities it expects to take in 125 students per year. The Des Moines Chamber of Commerce has given permission to the College to conduct a fund raising drive for the proposed new school. About 5-8 million dollars will have to be raised in Iowa if the College is to obtain Federal matching funds. There is *no* movement in Iowa for a merger of the two professions in the immediate future.

Maryland

Presently osteopaths may only obtain a limited license. There are only 19 osteopaths in this State. If amendments to the Maryland Osteopathic Act which have been proposed are enacted, an unlimited license would be available to DO's in Maryland.

New Jersey

There have been two successful lawsuits by osteopaths in New Jersey. In the first case the New Jersey Supreme Court on May 8, 1961, ordered the Middlesex County Medical Society to take into membership an osteopath who had been issued an MD degree by a foreign medical school, approved by the AMA, after he had attended the school for seven months.

In the second case a New Jersey Superior Court held on August 17, 1962, a hospital Bylaw was contrary to public policy to the extent it required membership in a county medical society as a condition precedent to courtesy staff privileges. The Court also held that a hospital Bylaw requiring graduation from a medical school approved by the AMA as a condition precedent for granting staff privileges to an osteopath with an unlimited license as contrary to public policy.

The Medical Licensing Board of New Jersey will not recognize the MD degree obtained by osteopaths from the California College of Medicine.

Pennsylvania

The Pennsylvania Medical Society has made a number of attempts to convert the Philadelphia College of Osteopathy in Philadelphia into a medical school. The Dean of the school is opposed to such a development.

The Pennsylvania Medical Society has taken the following steps to permit physicians to associate with osteopaths:

1. DO's are allowed to participate in postgraduate courses in the state.
2. MD's are permitted to consult with DO's.
3. DO's are allowed on the staff of MD hospitals provided they work under the guidance of MD's.

The Pennsylvania Medical Society believes that it has gone as far as it can with respect to bringing about an amalgamation of the two professions. The Society now feels that it is up to the osteopaths in that state to make some move in that direction if a merger is to be accomplished.

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The osteopathic society in Philadelphia took a poll of its members within the past year which revealed 80 per cent of its group favor a merger with the MD's.

A ruling has been issued by the Attorney General's office to permit an osteopath with an MD degree to take the MD licensure examination. It is the Committee's understanding that an osteopath with an MD degree from the California College of Medicine will take this examination in the near future.

In June 1964 the Board of Trustees of the AMA met with Dr. Samuel Newman, Chairman of the Committee on Osteopathy and Medicine, for a discussion of the future activities of the Committee.

The Board approved the requests of the Committee and authorized it to (1) continue to be available to (a) state medical societies which wish to explore methods by which to give MD status to osteopaths, and (b) osteopaths who wish to discuss mutual problems: (2) continue to keep abreast of MD-DO relations and to keep the states informed; (3) prepare articles and editorials on this subject for publication in *JAMA,* the *AMA News,* and other publications; (4) encourage the state medical societies to establish committees on osteopathy and (5) meet with representatives of the Federation of State Boards of Medical Examiners or with the editorial writers of the Federation's *Bulletin.*

The above material is a summary of what took place at the San Francisco meeting on June 21, 1964. Naturally, I have had to leave out a great deal. I have taken notes and I have several factual reports from the doctors who delivered these remarks. If any doctor is interested I will be glad to turn over my files to him or arrange to re-examine my notes to answer any questions which may arise from the material which I have submitted. I should like to thank the Council for allowing me to attend this meeting and wish to reiterate that any time the Council sees fit to ask me to attend a meeting I shall do my utmost to attend and present a report on it.

Respectfully submitted,
MAX CAPLAN, M.D.

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Around The State

New Haven County

BOARD OF GOVERNORS

September 24, 1964

The Board of Governors of the New Haven County Medical Association opened the fall season of 1964 with a meeting held at the Villa Capri, Wallingford, on September 24th, Dr. Jack Galen presiding. The lengthy session was devoted to reports of the Councilor and various committee chairmen which evoked general discussion.

A sum of money was voted to be used for Community Health Week (October 18-24) publicity in the newspapers of New Haven County.

Dr. Max Caplan was commended for his efforts in combating "Medical Quackery" and for his article in CONNECTICUT MEDICINE on that subject.

A letter from Dr. H. C. Hinchcliffe, Chairman of the Health Insurance Council was high in the praise of our Ad Hoc Committee, Dr. Kurt Pelz, Chairman, in resolving problems of fees involving insurance carriers and members. It was brought out that our approach is a realistic one that produces results with lessened friction between the parties involved.

Dr. Luca Celentano and his committee are revamping our life insurance structure to provide for eligibility without medical history.

New London County

On September 10th, the New London County Medical Association, through a grant by Lederle Laboratories, sponsored an all day symposium on gastro-intestinal diseases and infectious diseases, at the Norwick Inn in Norwich, Conn. The day's activities were well attended by over 135 physicians.

On October 1st, the Semi-Annual Meeting of the New London County Medical Association was held at the Norwich Inn. Honored guests were Ralph Gilman, M.D. President, Connecticut State Medical Society and William Richards, M.D., the General Manager.

The International Urological Congress

The thirteenth Congress of the Société Internationale D'Urologie was held in London August 29th to September 5th, 1964. About 350 members from 55 nations were in attendance. The United States was represented with 41 members. The program consisted of three subjects: Renal Insufficiency, Tumors of the Testis and Cancer of the Bladder. A report on one of thes subjects was presented every other day and general discussion was opened on the subject the following day. Movies played a prominent part in the program and were shown each day all day. The larger surgical clinics of London were hosts to the members and guests during three afternoons.

The British Urological Society and the British Surgical Society were hosts for several receptions and the ladies were provided with daily excursions to famous buildings and places of interest. The Congress was climaxed by a banquet at Guild Hall with the color and glamor after British Custom. The Lord Mayor of London in the absence for the Royal Family welcomed the Congress.

The program was stimulating and the British were most hospitable hosts. The Congress not only produced an interchange of medical scientific thoughts but most of all relieved some of the postwar tension between the Southern European countries and Germany by the selection of Munich as the next meeting place for the Congress. To be sure the Southern European countries have some reason for carrying a grudge but it has been twenty years since peace was declared for the Second World War. The plans for the 1967 meeting in Germany will do much to heal the wounds of the grieved nations. There is no doubt that medicine and medical science play a vital part in world peace.

CLYDE L. DEMING, M.D.

New Gastroscopy Film Awarded First Place

A color-sound 16 mm teaching film entitled "Eyewitness to Gastroscopy" has been awarded first place in the Institutional Category at the recent national competition of the Biological Photographic Association, Inc. held in New York City.

The film, written and produced by Dr. Martin E. Gordon, a New Haven gastroenterologist, was further honored recently by being selected for showing at the XIIth World Medical Congress in Helsinki, Finland.

The motion picture production was sponsored by the Hospital of St. Raphael, New Haven and supported by a grant from the Connecticut Division of the American Cancer Society. Thomas McCarthy of the St. Raphael staff was the photographer and Elliot H. Kone, Director of Yale's Audio Visual Center, the film editor.

The Evolution of Gastroscopy from the 17th Century Magenkratzer to the Laser is presented chronologically and the gradual development of the art is traced. The modern stroboscopic, biopsy and television applications with the principles of fiberoptics are outlined. The technique of cinegastroscopy permits the viewer to be an "eyewitness" to normal and abnormal intragastric views while the clinical aspects are stressed.

Future endoscopic potentials are shown, including the use of small Geiger counters, radiotelemetry, coherent light laser beams and other newer scientific frontiers.

This 26-minute film is scheduled to be released shortly for nationwide distribution to all hospitals and medical schools and may be obtained by applying to Martin E. Gordon, M.D., F.A.C.P., 111 Sherman Avenue, New Haven, Connecticut 06511.

Doctor's Office

Donald H. Badner, M.D. and Alfred T. St. James, M.D. announce their association in the practice of surgery with offices at 405 Broad Street, Meriden and 150 North Main Street, Wallingford.

Jerome S. Beloff, M.D. and Edward P. Wallace, M.D., announce that Irwin B. Bernhardt, M.D. has joined them in the practice of pediatrics and pediatric allergy at 71 Parker Avenue, Meriden and 181 North Main Street, Wallingford

Brendan M. Fox, M.D., announces the opening of an office for the practice of urology and genitourinary surgery at 140 Woodland Street, Hartford.

William Kessler, M.D., announces his association with Malcolm S. Beinfield, M.D. and William F. Hughes, M.D. in the practice of general surgery on Kings Highway, Westport.

Stanley E. Kilty, M.D., announces the opening of an office for the practice of internal medicine and cardiology at 167 Broad Street, New London.

Ludvic Joseph Pavlo, M.D., announces his association in the practice of medicine with Maria Margaret Pavlo, M.D. at 58 Minerva Street, Derby.

David P. Reed, M.D., announces the removal of his office for the practice of internal medicine and cardiology to 1389 West Main Street, Waterbury.

W. Tracy Scudder, M.D., announces the opening of an office for the practice of internal medicine at 750 Hopmeadow Street, Simsbury.

John S. Staneslow, M.D., announces the removal of his office for the practice of psychiatry to Summit Road, Prospect.

Measles Vaccine Studied In Eskimo Villages

Measles vaccines administered to Eskimos in Alaska where the disease is a serious problem produced a response similar to that found in other populations, a study showed recently.

The field trial was reported by Drs. Jacob A. Brody, Robert McAlister, Irvin Emanuel and E. Russell Alexander, Anchorage, in the current *Journal of the American Medical Association.*

"Our studies indicate that response to measles vaccine among Eskimos was similar to responses encountered in other populations, in spite of the fact that clinical measles is apparently more dangerous for these people," they said.

The severity of measles varies considerably in different areas of the world, according to the report. Early Arctic explorers reported devastating measles epidemics among Eskimos and Northern Indians. Today, measles remains a serious problem in native villages.

To determine whether reactions to measles vaccination were unusual among Alaskan Eskimos, Indians, and Aleuts, a series of studies was begun in early 1963 by the Arctic Health Research Center and the department of preventive medicine, University of Washington School of Medicine, Seattle.

The Eskimo villages of Chevak and Hooper Bay, located about 20 miles apart on the coast of the Bering Sea, were selected for the trials. The villages had escaped measles epidemics in the region in 1961 and 1962.

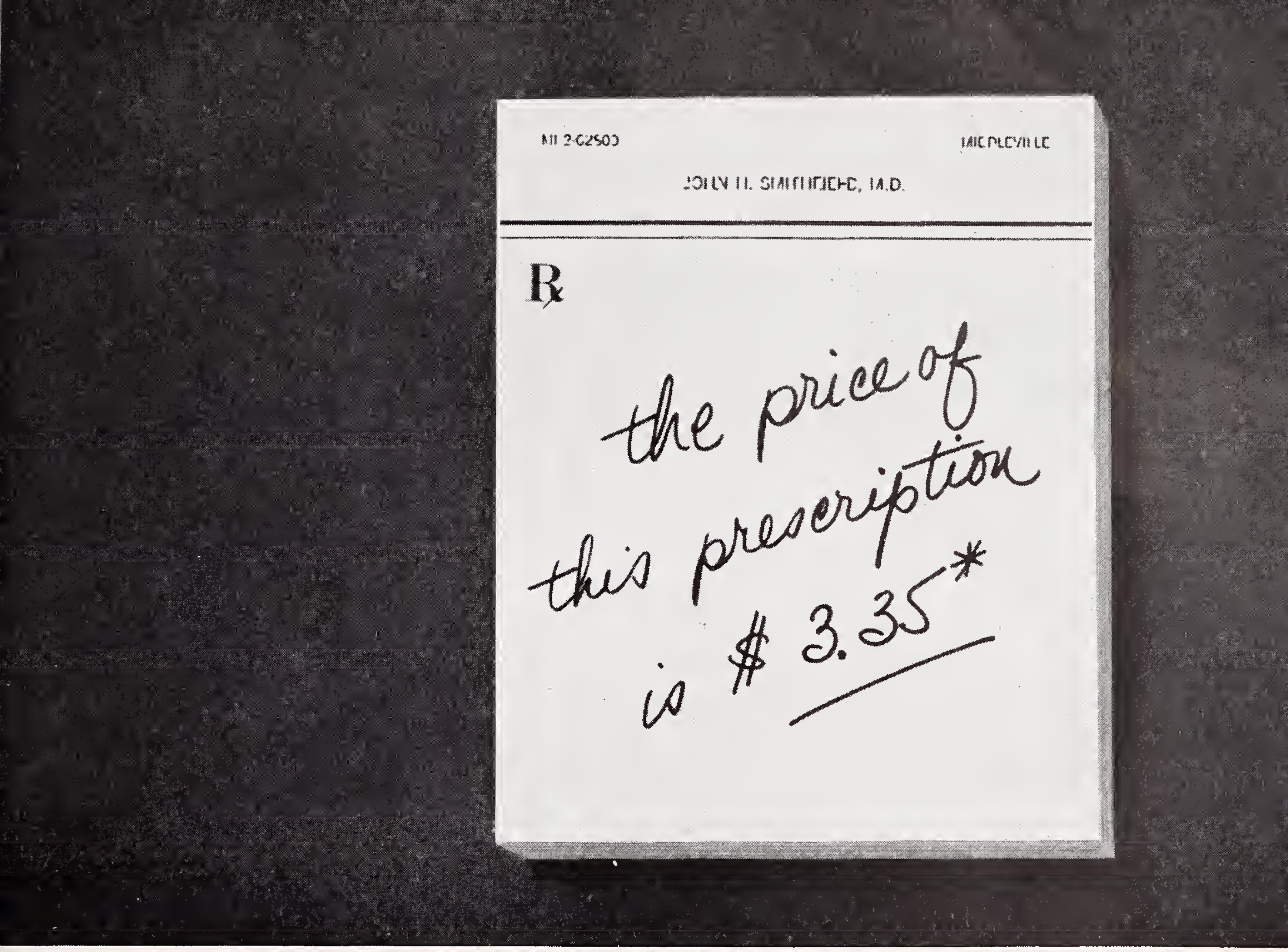
With a few exceptions, all children from six months to six years of age participated. In Chevak, live vaccine plus gamma globulin were given by injections. In Hooper Bay, one double-dose injection of killed vaccine was followed in six weeks by an injection of live vaccine.

Every other child received an inactive injection for comparison purposes. Examining physicians did not know which product a child had received.

In Chevak, 9 of 49 vaccinated children, or 18 per cent, developed a temperature of 103 degrees Fahrenheit or greater. In Hooper Bay, a temperature over 103 F occurred in 1 of 46, or 2 per cent.

"It is difficult at this time to draw conclusions concerning the methods and combinations of vaccination most appropriate for remote areas such as those encountered in Alaska," the physician commented.

Gamma globulin and live vaccine can be given in one visit, they said, but there is a risk of fever in 15 to 20 per cent a week to two weeks later. It is unlikely that trained personnel could remain in villages for the length of time necessary for the reaction phase to develop, they pointed out.



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Somewhat amazingly, $3.18 is correct. Even if you eliminated pharmaceutical manufacturer's net profit, your patient would pay only about 17 cents less for the average prescription—hardly a deciding factor in having it filled. Of course, this assumes that pharmaceuticals could continue to be available without profit (where do new miracle drugs come from, if not profit?).

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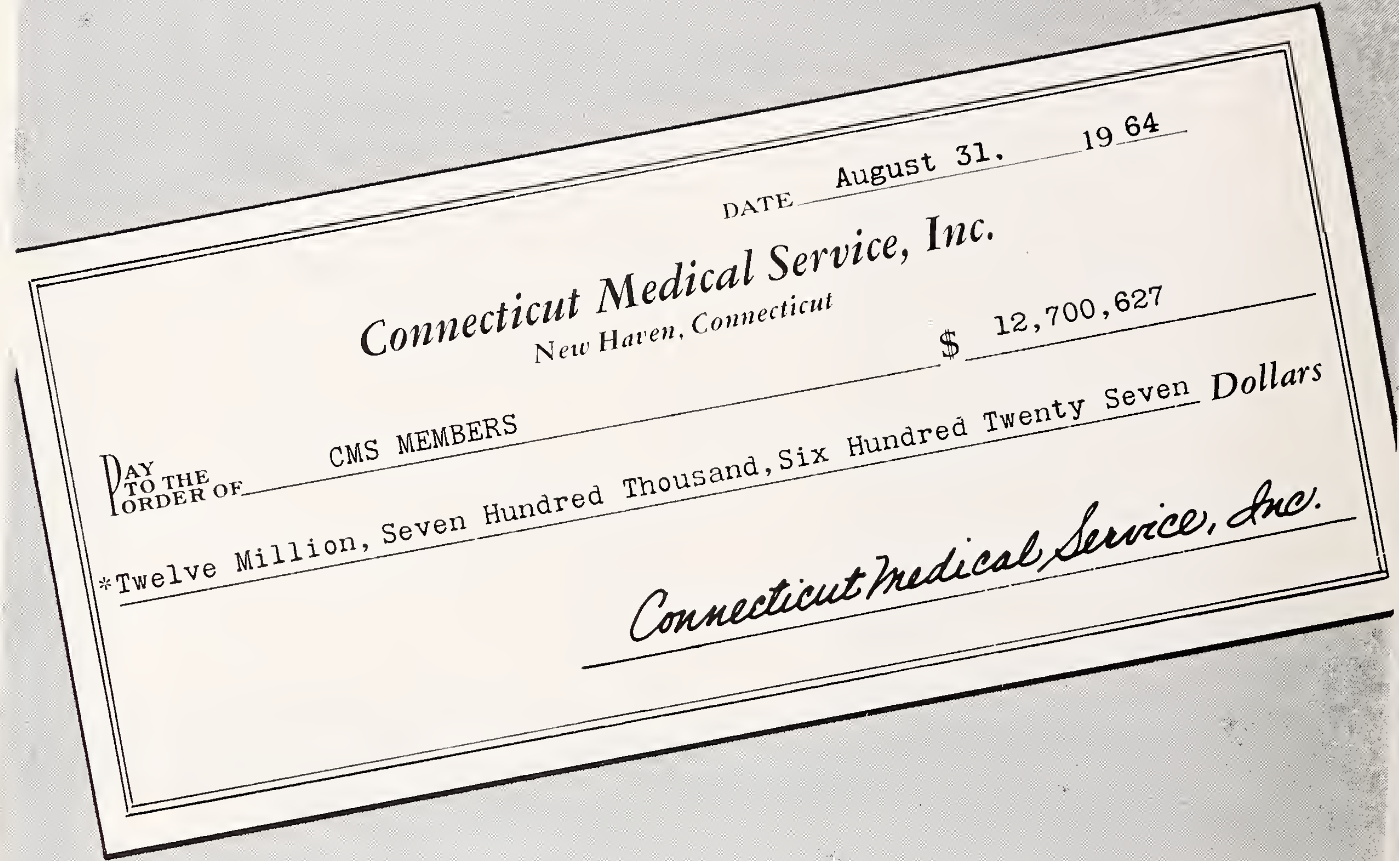
This message is brought to you as a courtesy of this publication on behalf of the producers of prescription drugs.

*Average prescription price, 1963. National Prescription Audit, R.A. Gosselin, Dedham, Mass.



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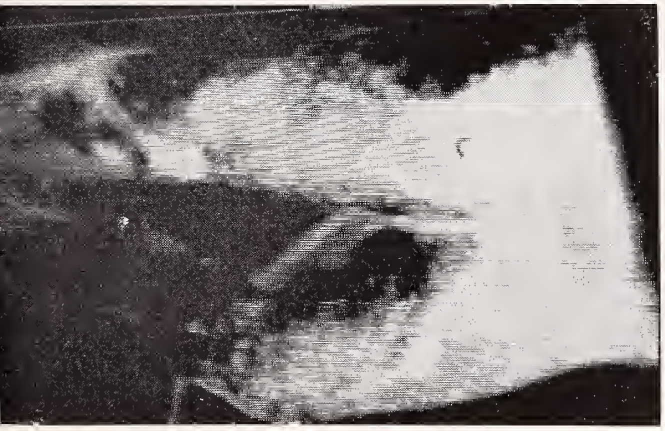
Letters To The Editor

To The Editor:

INFRARED THERMOGRAPHY

Infrared thermography, an electro-optical system, has been stablished as a promising medical instrument. This system s based on the fundamental concept that heat is emitted rom the surface of all objects. Every object, regardless of nolecular structure, has an emissivity constant. Therefore, rom the work of Hardy, we assume for practical purposes hat human skin is nearly unity when compared with a lack body whose emissivity is 1.0.

For the past year the Research Laboratory of this hospital as worked with a system that uses a thermistor bolometer etector that is sensitive to 0.001°C. Recording the data btained on Polaroid P/N 55 film, we have obtained "thermograms." The data can be very accurately interpreted because he thermal image seen on the emulsion is representative of 60,000 bit scan of the area of interest. From this photographic data, with the use of a densitometer, good quantitation of Δ-T can be established. The correlation with linical findings and diagnoses has been excellent.



At this time the instrument has shown greater specificity for localization of breast cancer. As an objective method for interpreting the joint involvement of rheumatoid arthritis, we believe it is the first known technique for this purpose. The follow-up on this is to do a controlled study on treated cases. To determine the area of burn degree, we believe there is no other comparable technique (Fig. 1). Note the area of third degree burn is "black" or "cold." Lesser degrees of burn depth are contrasting to "grey" or "white" or "hot." This illustrates the objectivity of the technique and should be of great help in burn management.

To localize bone tumors or metastatic bone lesions the themograph has been helpful. Brain tumors have been localized after the hair was clipped. (Hair is "cold" and obscures the heat pattern).

From many clinical centers and around the country reports are being published with regularity on the use of the thermograph in peripheral vascular disease, placental localization and breast cancer localization. This latter area of interest is now being studied in our laboratory. This has the support of the Connecticut State Cancer Society. A description of the study is the basis of this report.

Women are referred to the Thermograph Department who have passed their 35th birthday and have never had a diagnosis of breast cancer. A basic data sheet is completed which includes a breast history as described by Haagenson. After 10 minutes stripped to the waist in a room maintained accurately at 70°-72° F, a scan is performed in the anterior supine position. This scan takes 4 minutes with the improved equipment now available.

The resultant thermogram is interpreted blind by two observers and this data is recorded. All data is then sent for transfer to IBM cards for sorting and correlation. When the first 1,000 cases have been completed on IBM 1620 computer will then assemble the statistical material for study.

Throughout the study patients will be accepted who are known to have clinical cancer of the breast, but this information will be double blind to the observers. From the data published by the Breast Cancer study group in this state, our sample should yield between 5 and 7 cancers for the 1000 women surveyed. In this way we hope to establish efficacy of the thermograph and achieve a survey technique.

To complete our study we need the cooperation of interested physicians who will refer patients that fit the protocol. Appointments may be made by calling the Norwalk Hospital 203-838-3611, extension 609.

Warren Zeph Lane, m.d.

Norwalk, Conn.

EDITOR'S STIMULATION

To The Editor:

May I take this opportunity to commend you, again, upon the excellence of the editorials and to say that I find them the most interesting part of the *Journal*. I am always amazed at your wide comprehension of the multitude and great variety of subjects that are discussed in your columns. I hope your editorials will continue and always remain a prominent part of our *Journal*.

Sincerely yours,

Charles E. Jacobson, Jr., m.d.

Manchester, Conn.

Special Notices

WOUND INFECTION FORUM—HARTFORD HOSPITAL

October 16 and 17

A "Wound Infection Forum" was held at the Hartford Hospital on October 16 and 17, 1964. Important papers on this subject were presented by prominent investigators. It was sponsored by Davis and Geck Division, American Cyanamid Company of Danbury, under the auspices of the "Research Forum," Hartford Hospital Research Committee.

The major participants were: James G. Hirsch, M.D., Rockefeller Institute, New York, New York; Benjamin A. Barnes, M.D., Massachusetts General Hospital, Boston, Massachusetts; Robert S. Speirs, Ph.D., Downstate Medical Center, Brooklyn, New York; Edward L. Howes, M.D., Hartford Hospital, Hartford, Conn.; Balbina Johnson, Lecturer in Surgery, Columbia University, New York, New York;

George B. Ambrose, M.D., Presbyterian Hospital, New York, New York; Edgar J. Poth, M.D., University of Texas Medical Branch, Galveston, Texas; Stanley M. Levenson, M.D., Yeshiva University, New York, New York; Carl W. Walter, M.D., Peter Bent Brigham Hospital, Boston, Massachusetts; and John F. Burke, M.D., Massachusetts General Hospital, Boston, Massachusetts.

SECTION OF OPHTHALAMOLOGY OF THE SOUTHERN MEDICAL ASSOCIATION

November 16 — 19

The Section of Ophthalmology of the Southern Medical Association announces a most outstanding and interesting program to be presented this year at their annual meeting November 16-19, 1964 in Memphis, Tennessee.

The live television surgical program will feature cataract and strabismus surgery by Drs. Ralph S. Hamilton, J. Wesley McKinney and Daniel F. Fisher of Memphis, Tennessee and a panel of Ophthalmologists moderated by Dr. Philip M. Lewis of Memphis, chairman-elect of the section, and including Drs. William B. Clark of New Orleans, Louisiana; Louis J. Girard of Houston, Texas and DuPont Guerry, III of Richmond, Virginia.

The program will feature symposium on Retinal Surgery, Cataract Surgery and Corneal Surgery plus papers on Exophthalmos. The A and V Syndromes, Cystinosis and etc.

The chairman, Dr. Aibert C. Esposito, also announced that Dr. Harold F. Falls of Ann Arbor, Michigan will be the Guest Speaker at this year's meeting.

For additional information, please contact the secretary of the Section of Ophthalmology, Dr. George S. Ellis, 812 Maison Blanche Building, New Orleans, Louisiana.

A.M.A. CONFERENCE ON BLOOD AND BLOOD BANKING

December 11-12, 1964

The American Medical Association will sponsor a Conference on Blood and Blood Banking December 11-12, 1964, in Chicago (Drake Hotel).

The conference is directed to practicing physicians, said Gunnar Gundersen, M.D., chairman of the AMA Committee on Blood, expressing the hope that state and local medical societies will designate representatives to attend.

Objective of the conference is to "motivate the medical profession to evaluate and implement blood banking requirements and to participate generally in local blood banking affairs," Dr. Gundersen said.

Theme of the December conference will be: "Blood banking—Medical Evaluation and Participation." The program will include discussion of the different philosophies and concepts in the field of blood banking.

"The transfusion of blood when indicated is acknowledged to be life-prolonging therapy of the highest order," says an editorial prepared for the Journal of the AMA.

"To know when to administer, and how much, requires consummate clinical skill. To discern when transfusion is unnecessary or contraindicated is equally imperative."

The conference will be opened by Raymond L. White, M.D., director of the AMA's Division of Environmental Medicine and Medical Services, and by Dr. Gundersen. Louis K. Diamond, M.D., director of the Blood Grouping Laboratory, Boston, will outline the history of blood banking in the U.S.

A session on "Blood Banking Concepts and Systems," with Thomas D. Kinney, M.D., of Durham, N.C., as moderator, will include discussion of automation, central typing and crossmatching, medical sponsorship and supervision, a report on the Knoxville program, and hospital programs. Another session, with Charles C. Smeltzer, M.D., Knoxville, Tenn., as moderator, will cover the theme of Blood Procurement Concepts and Economics, including the areas of volunteer donor programs, paid donor programs, national clearinghouse program, and blood banking economics.

A session on "Blood Insurance-Assurance Plans," will be moderated by Clyde G. Culbertson, M.D., Indianapolis, Ind. A session on "Standards, Inspection and Accreditation," with Charles E. Rath, M.D., as moderator will open the second day of the conference, and will include a study of state laws and regulations.

Other topics on the conference program include studies of serum hepatitis and a discussion of single unit transfusions, blood research highlights, and medical responsibility and leadership in blood banking affairs.

Further information on the conference may be obtained from the Department of Environmental Health, American Medical Association, 535 N. Dearborn Street, Chicago.

SIXTH POSTGRADUATE MEDICAL SEMINAR CRUISE ALBANY MEDICAL COLLEGE OF UNION UNIVERSITY

January 6-20, 1965

A 14-day cruise from New York aboard the luxurious, stabilizer-equipped "M.S. Gripsholm." Ports of call are: St. Croix, Virgin Islands; Fort de France, Martinique, Barbados; Trinidad; St. Vincent, Dominica; St. Thomas. Faculty of Albany Medical College will present a comprehensive shipboard postgraduate program, covering subjects in internal medicine, pediatrics, obstetrics, gynecology, physical medicine, and surgery. The medical seminar constitutes 23 hours of Category I credit toward the postgraduate requirements of the AAGP. For information, write to: Department of Postgraduate Medicine, Albany Medical College, Albany, New York 12208.

EIGHTH ANNUAL INSTITUTE FOR PHYSICIANS IN INDUSTRY

March 8, 1965

The Program of Continuation Education of the Columbia University School of Public Health and Administrative Medicine announces the Eighth Annual Institute for Physicians in Industry. The one week course will be held at the Columbia-Presbyterian Medical Center complex in New York City during the week of March 8, 1965.

The institute is designed as an intensive refresher course relating to those subject areas of specific interest to physicians practicing in the field of occupational medicine. In addition, several sessions will be devoted to basic public health subjects. Physicians preparing to take specialty board examinations should find this institute particularly useful.

Further information and applications may be obtained from the Program of Continuation Education—Public Health, Suite 305, 21 Audubon Avenue, New York 32, New York.

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SEMI-ANNUAL MEETING
November 16, 1964
Hotel America, Hartford

The semi-annual meeting of the Woman's Auxiliary to the Connecticut State Medical Society will be held on Monday, November 16th at the Hotel America in Hartford. Registration starts at 10:30 A.M. with the business meeting following.

The special guest for the luncheon will be Mrs. Richard A. Sutter, President-elect of the Woman's Auxiliary to the American Medical Association.

The program committee has provided entertainment in the form of a "Hat and Fur Fashion Show" and a playlet, "To Temper the Wind," to be presented by the New London County Auxiliary members.

Reservation may be made with: Mrs. Joseph Wool, 803 Montauk Ave., New London, Connecticut.

Fall Conference

From October 4th through the 7th the Drake Hotel in Chicago echoed to the voices of the leaders of the Auxiliary to the A.M.A. The presidents and presidents-elect of the 50 State Auxiliaries learned not only *what* to know and talk about—they learned *how* to do it.

On Sunday, October 4th, women from all over the United States arrived by car, train, plane—even with their own self-piloted planes. They were entertained at a cocktail party—punch served only—and dinner at which Senator Everett Dirksen was the guest speaker.

On Monday, bright and early, coffee and rolls were served at 8:00 A.M. and the meeting started promptly at 9:00 A.M. The ladies were greeted by Dr. Donovan Ward, President of the A.M.A. and Dr. F. J. L. Blasingame, Executive Vice President of the A.M.A.

Then began a concentrated Speech Training Seminar conducted by Smith, Kline & French Laboratories under the guidance of Dr. Laverne Haakenson and four assistants. Approximately one year of a college course was covered in two hours and 20 minutes. Dr. Haakenson lectured on "Platform Effectiveness" and advised that a public speaker's objectives should be: 1. To be heard, 2. To be understood, 3. To be believed, and 4. To obtain ACTIVE response. After a number of additional terse and effective suggestions for greater speech effectiveness, drill sessions were held in small groups.

This course is available to groups of 25 or more as a public service free of charge. It was recommended for doctors who are needed to serve on speakers' bureaus as well as for their wives who are willing to present "Medicine's Story."

There followed an afternoon of leadership training with the slogan "She who dares to *Lead* must choose to *Learn*."

The chorus line technique was very effectively used in presenting the A.M.A.-E.R.F. projects. Some of our most charming doctor's wives sang and danced through the auditorium presenting "Miss

Christmas Card," "Miss Charmer," "Miss Correspondence," "Miss Playing Card," "Miss Tea Leaf," and the Queen herself, "Miss A.M.A.-E.R.F." These represented Christmas cards, 52 deck playing cards, charm bracelets and charms with medical insignia, correspondence paper in pink, blue, and white—all on sale for the benefit of the A.M.A.-E.R.F. and available through the County Medical Auxiliaries.

Two more early morning sessions followed with one full and one-half day of "education." A film, "Not As It Was," produced by the A.M.A. showing how doctors, as members of their local medical society and the A.M.A. have been able to bring better health care to both individual patients and their communities was shown. (This has been cleared for television showing and is available through the Connecticut State Medical Society.)

When the conference concluded at noon on Wednesday, the State Auxiliary Presidents and Presidents-elect voiced the opinion that they had learned much and hoped to pass on to other doctors' wives the enthusiasm, sense of responsibility, and knowledge gained here.

IMPORTANT NOTICE **IMPORTANT NOTICE**

Follow-Up Of Cancer Deaths

The Connecticut Tumor Registry of the State Department of Health will soon initiate a new procedure to obtain additional information on persons dying of cancer but never reported to the Central Registry while alive. Presently, ten per cent of all Connecticut's cancer cases are reported by Death Certificate only, indicating that these people were never hospitalized nor treated.

With the approval and upon recommendation of the Cancer Coordinating Committee of the Connecticut State Medical Society, physicians certifying a cancer death occurring in 1962 will receive an inquiry concerning their patient. This inquiry will contain four brief questions regarding diagnosis and treatment. It is the hope that the answers to these questions will further the research of the Registry into the etiology of cancer.

OBITUARIES

Irving S. Alderman, M.D.

1891 - 1964

The greater New Haven medical community records with sadness that Dr. Irving S. Alderman died at his home in New Haven August 26, 1964 after a brief illness.

Dr. Alderman was born in New Haven December 12, 1891 and was educated in local schools. His premedical education was obtained at Yale and after graduating in 1913 he continued at Columbia University, College of Physicians and Surgeons to earn his M.D. degree in 1917. Then followed two years internship at Bellevue and Lebanon Hospitals. Returning to New Haven he opened an office for the general practice of medicine and surgery and was engaged for many years in an active vigorous practice.

Following World War II, attuned to changing times and values, he gave up general practice and courageously embarked on a course of post-graduate education leading to eligibility for certification in the new discipline of Physical Medicine and Rehabilitation. He prepared for his new specialty practice at Yale and Columbia Medical Schools and served at the Rocky Hill and New Haven Hospitals. From 1952-55 he served in the Polio Clinic at New Haven Hospital. From 1950-1961 he was a member of the staff at the Hospital of St. Raphael and served from 1960-61 as acting chief of the Department of Physical Medicine with the title of Assistant Attending in Physical Medicine. In 1961 he was placed on the Emeritus List.

Dr. Alderman was a member of the local, county, and state medical societies and participated actively as a member of the Committee on Medical Ethics and Deportment of the New Haven County Medical Association. He was a member of the Connecticut Society of Physical Medicine. From 1917-19 he was a member of the U.S. Army Medical Corps.

Surviving Dr. Aldeman are his wife, Francis, three children and five grandchildren. His children include Dr. Melville Y. Alderman of West Hartford, Mr. Richard H. Alderman of New York and Mrs. Paul Naomi Winer of Woodbridge.

Irving Alderman will always be remembered as a devoted family man, loving husband and father, and as a hard-working dedicated physician, faithfully serving his patients in the old humanist tradition.

To the family of Dr. Alderman the medical community extends its deepest sympathy in this period of bereavement.

Samuel Climo, M.D.

James E. Davis, M.D.

1893 - 1964

Dr. James E. Davis, an ear, nose and throat specialist, died suddenly on August 9, 1964, at Hartford Hospital. He was 71 years of age.

Born in Marion, Virginia, he was graduated from Roanoke College and in Medicine from Johns Hopkins University. After interneship at Hartford Hospital he served West Hartford in general practice from 1921 to 1927. He then did graduate work in his specialty at the University of Pennsylvania, receiving an advanced degree.

From 1929 until his death he practiced otolaryngology in Hartford as a member of the Hartford Hospital staff—from 1950 with the rank of visiting otolaryngologist.

He was a diplomate of the American Board of Otolaryngology, a member of the American Academy of Ophthalmology and Otolaryngology and the New England Otolaryngological Society. Since 1922 he had been a member of the Hartford Medical Society, Hartford County Medical Association, Connecticut State Medical Society, and the American Medical Association.

For many years he was attending otolaryngologist at McCook Hospital, consultant to The Institute of Living and Manchester Memorial Hospital, and the Connecticut State Prison.

"Dr. Jim" was blessed with many friends throughout the greater Hartford area.

Dr. Davis is survived by two sons, James E. Davis, Jr., of Glastonbury and Donald B. Davis of Madison; a daughter, Mrs. Jacqueline Ahern of Bridgewater, Massachusetts, and nine grandchildren; also by his brother, Harold Davis of Charlotte, North Carolina.

MAURICE M. PIKE, M.D.

Nemo Dexter Gaines, M.D.

1901 - 1964

Dr. Nemo Dexter Gaines of Hartford, Connecticut, died at his home August 29, 1964. He was born in Elizabethtown, Illinois, January 25, 1901.

After receiving his B. of Ed. degree from the University of Southern Illinois, Carbondale, he obtained a B.S. degree from the University of Illinois. He graduated from the University of Illinois, College of Medicine, in the class of 1940.

Following internship at St. Mary's Group of Hospitals, St. Louis, Missouri, he practiced medicine in St. Louis, Missouri, Kingsport, Tennessee, and Houston, Texas, before moving to Hartford, Connecticut, to join the Travelers Insurance Company home office staff of physicians in 1942.

He was a member of the Connecticut State Medical Society and the American Medical Association, and belonged to the Harris County Medical Society of Houston, Texas, and Nu Sigma Nu medical fraternity.

He leaves his wife, Lucille Carter Gaines, a brother, Earl C. Gaines of Elizabethtown, Illinois, and a nephew, John Gaines.

The funeral was held September 1, 1964, at the First Baptist Church, Elizabethtown, Illinois, and burial was at the I.O.O.F. cemetery in that town.

John A. Pierce, M.D.

In Memoriam

Beauchamp, Maurice F.—Hamden; University of Vermont School of Medicine, 1943. Dr. Beauchamp was a prominent obstetrician and gynecologist in the New Haven area for 16 years. He was attending physician in obstetrics and gynecology at St. Raphael's and Grace-New Haven Hospitals. At one time, Dr. Beauchamp was a clinical instructor at the Yale School of Medicine, Department of Obstetrics and Gynecology. He was vice-president of the New Haven Obstetrical Society. Dr. Beauchamp was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the Connecticut Society of Obstetricians and Gynecologists, and the American Board of Obstetricians and Gynecologists. Dr. Beauchamp died September 23, at the age of 47 years.

Heinemann, Martin—New Haven; University of Goettingen, Germany, 1925. Dr. Heinemann had been a resident of New Haven since 1937 and conducted his medical practice at 210 Prospect Street. He was an Associate Clinical Professor of Medicine at Yale University School of Medicine. Dr. Heinemann died October 4, at the age of 65 years.

Drugs For Space Travelers

The problems of radiobiology or nuclear medicine pose some real challenges. Radiation injuries can be produced by many different sources; one of these is theoretically from ambient space radiation such as that encountered in the Van Allen belts. If space travelers, for various reasons, are required to spend protracted periods of time in these belts they may well need a drug which has anti-radiation properties. However, a more urgent need for anti-radiation measures is undoubtedly connected with nuclear devices which may be exploded in the earth's atmosphere. Recently Van Lancker, Wolf, and Mowbray at the University of Wisconsin have made significant progress in protecting primates from doses of 800 roentgens. Efforts are urgently needed to make available drugs which can be administered orally without toxic side-effects. This presents a major challenge to medicine, the biological sciences, and the military and civilian research organizations engaged in pharmacological research.—Brig. General Benjamin A. Strickland, Jr., USAF, MC, in *Military Medicine,* 129:1 (Jan.) 1964.

NEW BOOKS IN REVIEW

COMMUNICABLE AND INFECTIOUS DISEASES: Diagnosis, Prevention, Treatment, Fifth Edition, by Franklin H. Top and 25 Collaborators, 133 figures and 15 color plates. The C. V. Mosby Company, St. Louis, Missouri, 1964, 902 pp. $21.00.

Reviewed by: LOUIS H. NAHUM

This is the fifth edition and comes at a shorter interval than noted for any previous editions and rightly so because of rapid change in this field. Particularly in chemotherapeutic and antibiotic agents, in specific prevention of polio and measles, and in recognition of myocoplasmal pneumonia (formerly atypical pneumonia) as well as in adenovirus and the enterovirus infections.

New chapters have been contributed on malaria, on infectious encephalitis, on cocksakie and echo virus infections. There is revision of the chapters on impetigo, pediculosis, ringworm of the scalp and scabies. Primary atypical pneumonia, now called myoplasmal pneumonia, has changed materially and the chapter on respiratory infections has been altered greatly. There has understandably been a reduction in the size of the chapter on diphtheria and poliomyelitis now that these diseases have come under control.

The material is presented in a concise manner. Pneumococcus pneumonia tuberculosis, syphilis and gonorrhea receive extra attention, as they should because of their paramount importance both from curative and preventive aspects. The diseases are classified in a very interesting manner according to the portal of entry. There is little doubt that this method should prove helpful to students, even though there is overlapping.

The first section on general considerations applicable to communicable disease is followed by Section II in which the diseases are classified by the portal of entry, the respiratory tract, the gastro-intestinal tract, and mucus membranes and skin.

It is obvious that the book is intended as a text or handy reference for all persons whose professional duties necessitate contact with communicable disease or infestations. It is excellently written by national authorities and well illustrated. Each chapter is followed by a fine bibliography and an extensive index completes the volume. As usual, Mosby has done an excellent job in the format and printing. Even though there are twenty-five collaborators, the book is so well put together, that it reads as though from the pen of one author and for this Professor Top deserves great praise.

The next edition will doubtless come even sooner since the field is expanding rapidly. Much new knowledge on pharmacogenetics is offering explanations not only as to why some patients develop reactions from drugs, but also why some patients develop a disease in the first place while others similarly exposed do not.

SURGERY IN WORLD WAR II. Editor-in-Chief, Colonel John Boyd Coates, Jr., M.C., U.S.A. Activities of Surgical Consultants, Volume II, Editor, B. Noland Carter, M.D., 1964. 1062 pp. $8.50.

Reviewed by: DENIS S. O'CONNOR

The term "consulants" does not accurately connote the functions and activities of that higher echelon of medical experts which were peculiar to World War II. The term "supervisor" would have been more accurate but would have been hardly in keeping with the professional status of medical men. In appreciating a review of this volume on the so-called "surgical consultants" it would be well to keep this distinction in mind.

The idea of the consultant group was an excellent one and necessitated by the high degree of specialization in medicine which had taken place since World War I. In some high quarters of Army Medical Command it would seem as if this specialization was not appreciated and that the old concept that a "doctor was a doctor" still existed. The lack of properly trained medical personnel in the hospital sent to foreign theatres would seem to indicate this lack of understanding.

The consultants were expected to evaluate hospitals for efficiency, personnel for qualification in their respective specialties and adequacy of equipment; to educate the civilian specialist to application of his special knowledge to the changing needs of warfare; to provide educational opportunities for those whose specialized knowledge was incomplete; to keep medical personnel happy during periods of boring inactivity and exhausting overwork; to see that proper provisions were made for the medical care of the combat troops from the first aid level to the definite treatment of the base hospital. It was a big order but a review of this volume on the surgical consultants reveals an order of high accomplishment in all the major theatres.

The situation in the European Theatre of operations was ideal. The consultant organization was set up with the dispatch to Europe of the command of that theatre. Since actual warfare was still months in the future the consultants group had ample time to study their needs and plans for the invasion of the continent. Even the necessity of transport over the English Channel was of minor significance since return of casualties from the invasion coast was of short duration and it was a reasonable expectation that medical facilities on the continent could be set up shortly after the start of the invasion and that suitable buildings to house the hospitals would be available. It is no disparagement to Dr. Cutler and his consultant group to minimize the problems that faced them in that theatre. Dr. Cutler, as might be expected, did a superb job and some of the problems he faced were far from easy. Nevertheless the European Theatre was for all practical purposes "Army Country" with Navy assistance a minimum factor.

The Pacific Ocean Area, comprising several theatres at different times, was a different story. This was "Navy Country." The war was already in progress when most of the Army Medical Units arrived. There were many islands of various sizes involved with large areas of water separating them. The Army Table of Organization was too inflexible to allow for the few medical personnel which often would suffice, the unbreakable hospital or medical school hospital unit could not always be used to maximum advantage where located and it was difficult to know, except through an actual visit, to what extent medical facilities were being used efficiently. As in all theatres, some of the personnel were not professionally fitted for the positions which they held. Others were holding positions below their professional qualifications and all too often military rank did not coincide with professional ability.

Under the conditions which existed, transportation for the consultants was likely to be on a "hitch-hike" basis and it is remarkable that the chief surgical consultant was able to do as competent job as one must admit he did do.

When one realizes that the Pacific Islands in contrast to the permanent buildings and other appurtances of mature civilization, had only grass huts and malarial burdened mosquitoes one can appreciate what needed to be done to give these areas any semblance of what could be considered equal to camping out in our own country.

It was almost impossible to put the necessary medical personnel and equipment ashore in the early stages of an island invasion when the casualties could be expected to be high and it was only after the Army accepted the Navy system of getting the casualties back to the off-shore ships medically equipped that the early phase of medical care could be adequately handled. Even Ashore in the later phases frequently the lack of any buildings, such as we know them in our modern world, reduced the Army to tent and underground structures. The lack of any docking facilities made the transportation of heavy equipment, such as electric generators, almost impossible.

The problems of the Surgeon General's Office were great due to factors outside the actual functioning of that office, mention of which has been made in other reviews, but certainly the organization set up which was so ideal for the European Theatre could not have been expected to function under the conditions which existed in the Pacific Area. Either a Navy-type medical organization should be adopted or the Army medical personnel should be integrated into the Navy Landing Operations. Medical grouping of varying numbers and qualification should be available at a suitable staging area to be sent to any land area where the need for an organization appears needed rather than to send a fully equipped hospital when a need does not exist.

The India-China Area presented still another problem. India presented the only entry to the area and the distances to China were great with inadequate transportation. The fighting forces in China were the Chinese themselves and their doctors represented an era long since past. It was almost impossible to bring present day medicine to this area and in spite of the efforts of the consultants to that area the war had finished before their wants were recognized.

Whatever criticism of the functioning of medical coverage as portrayed in this volume, there can be no criticism of the consultant concept nor of the conduct of the consultants. It can be hoped that the concept which is excellent will be developed and refined and adapted to any area or geographical situation which presents itself militarily.

The difficulties of making military rank coincide with professional ability are insoluble. It seems incomprehensible that anyone in time of national danger would fail to give the full measure of his abilities without regard to his military rank.

CANCER OF THE STOMACH by William H. ReMine, M.D., M.S. in Surgery, F.A.C.S.; James T. Priestley, M.D., M.S. in Experimental Surgery, Ph.D. in Surgery, F.A.C.S.; Joseph Berkson, M.D., D.Sc.; and members of the staff of the Mayo Clinic. W. B. Saunders Company, Philadelphia and London, 1964. 255 pp. $11.50

Reviewed by: IRA S. GOLDENBERG

Although gastric cancer is one of the more common malignancies treated in American hospitals, there are few institutions able to report a 52-year experience with almost 12,000 surgically treated patients. The clinic at Rochester, Minnesota, founded by the Doctors Mayo is probably the sole center in the United States able to undertake such a task and perform it with skill and brilliance. Not only are exhaustive statistical correlations reported in this slim second edition (the first was published in 1942), but the authors also detail the areas of historical background, diagnostic measures, anesthetic problems and step-by-step surgical techniques of several operations, and present an analysis of the pathological aspects of gastric cancer. The fourteen contributing authors have written succinctly and ably and the text is illustrated with clear black and white and some beautiful color plates. The world literature has been searched with diligence and a complete bibliography accompanies each specialized chapter.

The epidemiological factors of this disease are fascinating and this book is somewhat marred by the absence of any discussion of this aspect. What a wonderful addition would have been a chapter devoted to discussion of possible reasons why gastric carcinoma develops in certain populations and not in others; and, even more intriguing, why the disease seems to be less frequently seen in the 1960's in the United States than in decades past.

In the presentation of survival data, Dr. Berkson unfortunately does not utilize the actuarial or life table method which is now becoming standard for reporting cancer data. In fact, he does not detail how survival data were derived but refers the reader for particulars to the previous edition of this book which was published twenty-two years ago. Statistical methodology has become increasingly sophisticated during the past two decades and employment of modern data processing equipment has opened new and meaningful avenues of analysis which Dr. Berkson does not utilize.

This volume is, as usual with any W. B. Saunders publication, a good example of the best in printing craft. It is particularly valuable to the surgeon treating gastric cancer but is excellent also for other physicians who want to go to one of the most complete source books available for information about gastric cancer.

VISTAS IN NEUROPSYCHIATRY. Edited by Yale Davis Koskoff and Robert J. Shoemaker, University of Pittsburgh Press, Pittsburgh, Pennsylvania, 1964.

Reviewed by: LOUIS H. NAHUM

This book is obviously designed to reflect the revolutionary changes which have taken place in the field of neuropsychiatry over the last fifty years, since the Pittsburgh Neurological Society was founded in 1912. At that time it was devoted to neurology, now we find neurophysiologists, neurosurgeons and psychiatrists as well. This fact of itself indicates a search for some unitary principle to encompass body and mind. It further recognizes the value of bringing these scientists engaged in these disciplines together for the enrichment of all.

Markedly dynamic changes have occurred in the behavioral success in the last fifty years; we now have more character and behavior disorders and defective interpersonal relationships and less hysterias. Manic depressive psychoses are less common. Schizophrenias are less pernicious. There have also occurred changes in society's attitudes toward mental illness, so that physician as well as social agencies look more and more to the psychiatrist for assistance. Patients are now being handled more and more outside mental hospitals and medical schools have given a larger place to psychiatry.

Many methods of therapy such as insulin coma, prolonged narcosis, psychosurgery, all had their vogue. Drugs have hastened the disappearance of all but electroshock. But none of these vogues has brought any new understanding of mental or emotional illness. There is no doubt that psychopharmacology has gained ascendancy in the treatment of mental illness, with its tranquilizers and energizers, but how much have they assisted in the investigation of mental illness itself? The mere fact however that the patient has come to be treated as a sick human being, not as one possessed by the devil; that the psychiatrist has become a participant in a variety of community agency operations, in the law, is recognized as a citizen expert possessing particular skill and experience, has called forth increasing support for research in psychiatry.

Much primate research has served to document hypotheses dearly held by psychoanalysists and has helped neurophysiologists to obtain data concerning the cerebral substrata of behavior. The growth of molecular biology has opened to investigation the basis of memory traces.

The articles in this book have much to say on all these matters and are written by national and international authorities. E. Earl Walker on neurophysiology, H. W. Magoun on memory processes, H. H. Harlow on social deprivation in monkeys, A. S. Marrazzi on a theory of psychosis bases on failure of cerebral homeostasis, Henry W. Brosen on vistas in psychotherapy, M. Raydon C. Astley on religion and psychiatry with discussion by representatives of the three faiths. There are three papers on the use of drugs, one by Mortimer Ostow attempts a theoretical analysis of the reasons for success and failure in drug therapy based on the assumption of increase and decrease in libido. A. S. Watson writes on family law and its challenges for psychiatry and Jack A. Wolford on social psychiatry in Pittsburgh 1962. Finally, there is a brief story of the Pittsburgh Neuropsychiatric Society.

It is fortunate that Dr. Yale D. Koskoff was president of the society on its golden anniversary and senior editor of this volume. The concept of such a volume and the enlistment of great scientists to contribute to it, deserves high praise. Dr. Koskoff will be remembered as a native of New Haven, educated at Yale, the first American assistant to the famous Dusser de Barenne, an investigator of note, especially in the new area of hemispherectomy and a designer of a valuable sterotaxic instrument for chemopallidectomy which was published in our journal.

OCULAR AND ADNEXAL TUMORS, Edited by Milton Boniuk, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1964, 502 pp., 363 figures and 4 color plates, $25.00.

Reviewed by: R. M. FASANELLA

This book is based on a symposium sponsored by Baylor University College of Medicine, covering especially the new and controversial aspects of ocular tumors.

It is written especially for ophthalmologists but will also prove of great interest to radiotherapists and of limited interest to pediatricians, neurosurgeons, physicists and general practitioners.

The conference is well organized with fine contributors and the book offers a pleasing format and good index.

The lectures and especially the discussions will reward the clinician with a review of all that he may have heard or read in journals and bring him up to date on knowledge of lid and conjunctival tumors, retinoblastoma, pigmented intraocular tumors and orbital tumors.

Many of the figures have been taken from colored slides and are not as effective, from a teaching standpoint, as the drawings more of which the reader would enjoy.

The reader, especially the practicing ophthalmologist, with clinical problems will enjoy the "pearls" offered by the seventeen contributors and will find in this text the answers to many old and new cases that he has or will encounter in his practice.

EPISODE. Eric Hodgins. Atheneum, New York, 1964. 272 pp. $5.00.

Reviewed by: F. W. GOODRICH, JR.

This is the story of a man's struggle for recovery from a cerebrovascular accident, a mental depression, and a fractured hip which occurred seriatim and necessitated 160 days hospitalization over a period of nineteen months. The author, a professional writer for many years, is perhaps best known for his novel, "MR. BLANDINGS BUILDS HIS DREAM HOUSE." If "EPISODE" receives the attention that it deserves, it will be in print long after MR. BLANDINGS and his other novels are gathering dust on the back shelves of the used-book stores.

It is not often that we who take care of sick people have the opportunity to see ourselves as patients see us. It is even rarer to have this view presented in a literate fashion, factually, objectively as possible under the circumstances, and without rancor. When such an opportunity occurs, we had better take advantage of it if we make any pretense of being humanitarian.

Although Mr. Hodgins encountered enough unthinking doctors, unfeeling nurses, and inhumane hospital routines to make him bitterly resentful, this is not simply a diatribe against modern medicine. It is not an account which the reader can brush off because, "that kind of thing doesn't occur in our hospital or my practice." It is an account of one man's suffering through a prolonged series of physical and emotional catastrophes which could happen to any of us. It is told without self pity but with humor and it is told by an acute observer. Those who care for patients will learn much that is missing from textbooks and modern curricula about the process of recovery from a stroke, a depression, and a fractured hip.

All of us need reminding of the tremendous cost of medical care. Mr. Hodgins illnesses cost him $21,911.32 of which just $7,891.3 was paid by insurance. We also need reminding that doctors can unnecessarily add to the cost by blind adherence to routine.

This book should be required reading for all students in the health professions. It should also be required reading for graduate practitioners of the healing arts. It should give us all to think.

MEDICAL NEWS

Study Size Of Hospital, Staff In Psychiatric Care

A comparison among 30 Veterans Administration hospitals indicates that psychiatric treatment is more effective in the smaller, more highly-staffed institutions.

The study, reported by Leonard P. Ullmann, Ph.D., Urbana, Ill., and Lee Gurel, Ph.D., Washington, D.C., confirms the general belief that smaller size and higher staff-to-patient ratio are related to higher rates of favorable outcome.

The findings further tend to show that these two factors influence different aspects of treatment and have different areas of impact, the researchers wrote in the current Archives of General Psychiatry, published by the American Medical Association.

"Both small size and high staffing were significantly associated with hospital effectiveness," they said.

"Small size was found to be of greater importance in establishing a high rate of early release, while high staffing was found to be of greater importance in obtaining turnover in terms of number of admissions, number of terminated cases, and percentages of patients with long-continued hospitalization.

"The data dealing with size support the trend to build smaller hospitals, or if this is not feasible, to utilize unit system plans.

"The data dealing with the effect of staffing on turnover criteria as distinct from early release may be taken as an indication of the value of increased staffing on continued treatment, chronic, or backwards, rather than the current possibly disproportionate emphasis on staffing of acute or admission wards."

VA hospitals are typically smaller and more highly staffed than state mental hospitals, it was pointed out. The size of the 30 hospitals in the study, based on the average daily patient load, ranged from 604 to 2,390 patients with an average of 1,453.

Hospitals were selected which had a high percentage of psychiatric patients. The 7,212 patients studied consisted of every male schizophrenic under 60 years of age admitted during the first year of the two-year study who later established an unequivocal early or late "first significant release."

Effectiveness of hospitalization was based on four criteria — early release, admissions, turnover, and long hospital residence. The four factors were highly correlated, i.e., the more early releases there were, the greater the space available for new patients, the lower the percentage of inpatients with long stay, and the higher the turnover as measured by terminated cases.

For all age and marital status categories, smaller hospitals had a higher rate of early releases than larger hospitals, the researchers also reported.

Smaller hospital size was particularly important with the patient group with poorest likelihood of early release, men who had never married, they said, adding:

"The difference between small and large hospitals in the rate of early [release] . . . of older single men was, perhaps, the most impressive single finding of this study because these are the men most likely to become continuously hospitalized and forgotten."

The study was completed as an individual hospital project within the Veterans Administration Psychiatric Evaluation Project. Dr. Ullmann is affiliated with the department of psychology, University of Illinois.

Blood Pressure

The ups and downs of your blood pressure help to forecast the state of your health, somewhat like the readings of a barometer help to forecast the weather.

If the arterial blood pressure becomes too low to circulate the blood properly, certain vital organs, particularly the brain, fail to function. Dizziness on standing, fainting or cold skin may be due to blood pressure that is too low for your body's needs.

High blood pressure, properly called arterial hypertension, is an abnormal state of the circulation that may be a cause as well as a result of arterial disease.

Hypertension appears to be a complex of influences from our inheritance, emotional life, diet, stress, exercise and the body's response to the vicissitudes of life. A disease of this nature hardly can be expected to respond to a pill or a potion or be cured by a single course of some panacea.

Hypertension requires a lifetime of management. The patient and his doctor, working together, plan a living pattern, supplemented by various medical procedures, that will result in the longest and most useful life the patient can live.

In dealing with hypertension, first there must be a medical history and a complete physical examination. Therapy often includes various medications which your doctor prescribes. Diet and weight control may be an important part of the treatment. And a planned way of life often is essential, involving hours of sleep and exercise, periods of rest and frequent vacations away from the problems of home and the stress of business.

Blood pressure tends to increase with age. High blood pressure will ultimately produce disabling or fatal complications. To help prevent complications, long-time management must be planned.

It is highly important in combatting hypertension that there be close rapport between the patient and his physician. It is essential that the patient understand his disease, know the need for continued treatment and be willing to tolerate the occasional unpleasant side effects of some of the drugs used. The patient must look to the long-term good to be obtained.

High blood pressure may continue for years before any serious physical symptoms show up. Thus it is important to have regular physical checkups, so that your doctor can detect any abnormalities of blood pressure early and begin therapy.

Anticoagulants In Coronary Artery Disease

The use of anticoagulants to reduce thromboembolic complications following myocardial infarction and to prevent coronary thrombosis in patients with angina is the subject of sharp controversy. Many eminent clinicians are convinced that anticoagulant therapy during the six weeks or so of the acute phase of infarction saves many lives by reducing the risk of venous and mural thrombosis, embolism and new myocardial infarctions; some of them believe that mortality from coronary artery disease can be further reduced by lifetime use of anticoagulants after infarction or in patients with severe angina. Some favor anticogulant therapy only in "high risk" patients, that is, those with severe infarction, heart failure or serious arrhythmias. Other clinicians, equally eminent, find no justification for the routine use of anticoagulants during either the acute phase of myocardial infarction or subsequently.

Although the number of reports favoring the use of anticoagulants is much greater than the number opposed, none are based on studies large enough and sufficiently well controlled to permit a resolution of the controversy. In this situation, what course should the physician follow in treating a patient who has just suffered a coronary thrombosis or who has angina or coronary artery insufficiency? Until the controversy is resolved, should anticoagulants be used? This is the question The Medical Letter sent out to answer with the aid of its consultants.

While The Medical Letter generally does not publish reviews of the literature on drug therapy, the lack of a clear consensus on anticoagulant therapy makes a brief summary of the principal studies desirable. The reader should keep in mind the fact that among the studies there is great variation in the application of clinical and statistical controls and in the criteria which were used in the clinical diagnosis of thromboembolism.

SHORT-TERM STUDIES—The most detailed, if not the best controlled, short-term study of the effects of oral anticoagulants on the course of acute myocardial infarction was reported by the Committee on Anticoagulants of the American Heart Association (I. S. Wright, C. M. Marple and D. F. Beck, "Myocardial Infarction," New York: Grune and Stratton, 1954). More than a thousand patients participated; their assignment to the treatment group and the control group was not random but depended solely on whether they entered the hospital on an odd or an even day of the month. The death rate in the control group during the six-week period of the study was 23.4 per cent, in the treated group 16 per cent, a difference which was found to be statistically significant, and was related to a reduction in thromboemboli complications.

H. J. Lockward, et al. (Public Health Rep., 78:655, 1963) made a retrospective short-term study of the effects of both anticoagulant therapy and intensive hospital care in the mortality rates of 175 patients with myocardial infarction with groupings by age, sex, degree of risk, type of hospital care (intensive vs. conventional) and use of anticoagulants. Anticoagulant therapy was reported to have reduced the mortality rate by 28 per cent (15 per cent fewer deaths occurred in the intensive-care group than in the conventional-care group).

The study most frequently cited in support of the case against short-term anticoagulant therapy is that of T. Hilden, et al. (Lancet, 2:327, 1961). This study showed an incidence of thromboembolism, established clinically or by autopsy, of 15 per cent of the treated group as compared with 25 per cent in the control group, a difference found to be significant. There was practically no difference in the total deaths, however—23 per cent in the treated group as against 25 per cent in the control group. Truly random assignment of patients was not observed, and there is doubt as to the adequacy of anticoagulant control.

LONG-TERM STUDIES—B. Manchester (Ann. Intern. Med., 47:1202, 1957) studied 204 patients under treatment and 200 placebo controls continuously for from one to 10 years and reported that mortality rate in the treated group was one-eighth that of the control group. Controls were inadequate.

A better controlled long-term study was that of C. J. Bjerkelund (Acta Med. Scand., Vol. 158 [Suppl. 330], 1957). All patients with myocardial infarction received therapy with oral anticoagulants for about one month, then 237 were assigned alternately to a treatment group and a control group. They were studied for periods of two-and-a-half to four years. During the first year, there was one reinfarction and two deaths among treated patients under age 60, compared with nine reinfarctions and eight deaths in the control group. These differences were found to be statistically significant. After the first year, however, the differences were not significant. After seven years of study, Bjerkelund concluded (in Anticoagulants and Fibrinolysins, Philadelphia: Lea & Febiger, 1961, p. 266) that lifelong treatment with anticoagulants was not yet justified.

The Working Party on Anticoagulant Therapy in Coronary Thrombosis of the British Medical Research Council (Brit. Med. J., 1:803, 1959) employed more rigid criteria for selection of cases, assignment to groups by true random procedures and not simply by alternation, and a detailed accounting of losses in each group. A single-blind design was used, with the treatment group (195 patients) given full-dose phenindione tablets and the control group (188 patients) placebo doses of phenindione. The rate of reinfarction in the treated group was one-fifth that in the control group under age 55, and one-half for those aged 55 and over. The death rate for the first three months, but not in the subsequent 16 months, was significantly lower in the treated group.

B. Harvald, et al. (Lancet, 2:626, 1962) conducted a trial on a total of 315 patients with observation over a period of several years and found no differences in the mortality rate between the treated and the non-treated groups during the first year or during subsequent years. There was a significant difference, however, in the thromboembolism rate, 0.23 per 100 patient-months of exposure in the anticoagulant group and 0.52 in the placebo group.

A. J. Seaman, et al. (JAMA, 189:183, July 20, 1964) carried out a double-blind study over a seven-year period on 66 patients in the treatment (phenindione) group, 67 in the placebo group, and 63 in a non-treated third group of "known control patients." Each group was composed of patients who had had a myocardial infarction at least eight weeks previously. Initial anticoagulant therapy was given to all three groups for a period of six weeks. The trend of the sequential analysis of this long-term continuing study is in the direction of demonstrating "no difference" between treated and untreated groups with respect to death rate or incidence of thromboembolism.

ANTICOAGULANTS IN ANGINA—There are few studies concerned with the ability of anticoagulants to prevent first infarction. In one study, which was not double-blind, C. F. Borchgrevink (Acta Med. Scand., Vol. 168 [Suppl. 359], 1960; Lancet, 1:149, 1962) reported on 147 patients under age 70 with a history of angina pectoris of less than two years and more than four weeks duration and without infarction. One group received intensive anticoagulant therapy, and a control group received anticoagulants at what amounted to a placebo level of anticoagulation. Patients with angina pectoris had significantly lower infarction and mortality rates on intensive antcoagulant therapy than on placebo therapy.

RISKS OF BLEEDING—In most of the long-term studies, death rates are based on deaths from all causes, including hemorrhage. The risks of hemorrhage from treatment are considerable; fatal cerebral hemorrhage occurred in four of Bjerkelund's 118 treated cases. Such complications cannot always be prevented, even by meticulous control of prothrombin time (J. W. Pollard, et al., Circulation, 25:311, 1962). In a preliminary report on a Veterans Administration Cooperative Study (R. V. Ebert, Address to the American College of Physicians, 1963), the incidence of bleeding was stated to be over 50 per cent. Most of the hemorrhages were of no clinical importance; but some were serious, and two patients died.

IMPORTANCE OF CONTROLS—As pointed out earlier, and as reflected in the studies cited, the number of reports favoring the use of anticoagulants is much greater than the number opposing such use. Scientific issues are not settled by comparing numbers of reports, however, especially when controls are lacking or inadequate. Some elements of control, such as matching size of groups, sex, age, and severity of illness, are described in most of the reports published since 1954, but truly double-blind studies with all important variables controlled are rare. The need for double-blind procedures may seem far-fetched when objective measurements of the clinical course of coronary artery disease are available, and when mortality rate is the final determinant of the success of therapy. Experience has shown, however, that for a variety of reasons, the lack of double-blind procedures greatly increases the likelihood of unreliable results even with objective measurements. With anticoagulant therapy, such procedures become doubly important since patients taking anticoagulants may receive more intensive medical supervision than those receiving placebos.

PSYCHOLOGIC FACTORS — Intensive care means greater opportunity for the physician to correct unfavorable environmental or other factors influencing the course of coronary artery disease, to detect complications more promptly, and to strengthen morale. Emotional factors associated with a physician's close care may be of great importance in coronary artery disease, as they are in many other diseases. The confidence a physician feels about a treatment may contribute to its therapeutic benefits, even in organic disease. Furthermore, knowledge that a patient is receiving anticoagulants may cause unconscious bias in the diagnosis of thromboembolism. Hence, the most carefully designed controls are needed despite the availability of objective determinations. None of the reported studies meet all the requirements for a well-controlled trial. Hopefully, the results of the U. S. Veterans Administration Cooperative Study and the follow-up studies of the British Medical Research Council, when they are reported, will provide more reliable data than are now available.

CONCLUSION — On the basis of the present data, what course should the physician follow? The Medical Letter believes that the totality of the evidence favors anticoagulation during the first six to eight weeks after an infarction, when it may be helpful in controlling venous thrombosis, clots within the heart chambers and embolism to the lungs and other organs. A case can also be made out, though with lesser assurance, for the use of anticoagulants in male patients under the age of 55 during the first 9 to 12 months after infarction. For older patients, and for treatment continued beyond the first 9 to 12 months, benefits are more questionable. The evidence thus far does not permit any confidence in the value of anticoagulation in preventing first infarctions in patients with angina. If close medical supervision is not practical, if the patient is not likely to be cooperative, if facilities for careful control of clotting factors are inadequate, or if there is a history of peptic ulcer or other diseases with hemorrhagic tendencies, then anticoagulants should not be used for either short-term or long-term therapy.

Antibiotic Dosage In Staphylococcal Enterocolitis

In its appraisal of antibiotic treatment of enterocolitis caused by resistant staphylococci, The Medical Letter (6:61, July 31, 1964) said that a single *oral* dose of vancomycin (Vancocin—Lilly), kanamycin (Kantrex—Bristol) or ristocetin (Spontin—Abbott), given daily for several days, could be effective in controlling the infection. These drugs are likely to be more effective, however, if they are given in doses of one gram *orally* every hour for four hours, followed by one gram every four hours for several days or until the staphylococci disappear from the stool. The Medical Letter also recommended as equally effective, methicillin (Staphcillin — Bristol; Dimocillin-RT — Squibb), oxacillin (Prostaphlin — Bristol) and nafcillin (Unipen — Wyeth), the first intramuscularly, the others either intramuscularly or orally. All these drugs should be used in doses of at least one gram every four hours until the diarrhea ceases and the staphylococci disappear from the stool.

Reprinted from The Medical Letter on Drugs and Therapeutics, *New York, N.Y., Vol. 6, No. 18, August 28, 1964.*

Rejoining Severed Arm Worthwhile For Some

Replantation of severed arms is a worthwhile procedure for certain patients under certain circumstances, two Boston surgeons recently revealed.

The restoration of arms in two patients, a 12-year-old boy and a 44-year-old man, was reported by Drs. Ronald A. Malt and Charles F. McKhann in the current Journal of the American Medical Association.

"Functional recovery in the arms has now made it clear that replantation in selected cases is a worthwhile procedure," they said.

for the ulcer life:

a new strength of glycopyrrolate

ROBINUL® FORTE

2 mg. per tablet

ROBINUL®-PH FORTE

glycopyrrolate 2 mg. phenobarbital 16.2 mg. (warning: may be habit forming)

When glycopyrrolate was first introduced, clinicians were immediately impressed by the emarkable ability of this compound to exert a more specific pharmacologic action on the gastrointestinal tract than on other organ systems. For example, they often found that in difficult patients the dosage could easily be adjusted upwards to achieve the desired suppresion of both hypertonicity and secretion . . . without paying the penalty of side effects intolerable to the patient. Thus, it is no surprise that many clinicians suggested that a double-strength 2 mg. tablet of glycopyrrolate would be both practical and useful. For those patients ordinarily unresponsive to anticholinergics or for those exhibiting the more prominent sympoms, the new Forte dosage forms are a worthwhile addition to your ulcer armamentarium.

BRIEF SUMMARY

NDICATIONS: In addition to its primary indications for duodenal and gastric ulcer, glycopyrrolate is indicated for other G-I conditions which may benefit from anticholinergic therapy. Robinul-PH Forte (glycopyrrolate 2 mg. with phenobarbital) is ndicated when these situations are complicated by mild anxiety and tension.

CONTRAINDICATIONS: Glaucoma, urinary bladder neck obstrucion, pyloric obstruction, stenosis with significant gastric retention, prostatic hypertrophy, duodenal obstruction, cardiospasm (megaesophagus), and achalasia of the esophagus, and in the case of Robinul-PH Forte, sensitivity to phenobarbital.

PRECAUTIONS: Administer with caution in the presence of incipient glaucoma.

SIDE EFFECTS: Dryness of mouth, blurred vision, urinary difficulties, and constipation are rarely troublesome and may generally be controlled by reduction of dosage. Other side effects associated with the use of anticholinergic drugs include tachycardia, palpitation, dilatation of the pupil, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, drowsiness, and rash.

DOSAGE: Should be adjusted according to individual patient response. Average and maximum recommended dose is 1 tablet three times a day: in the a.m., early p.m., and at bedtime.

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The boy, whose right arm was rejoined below the shoulder in 1962, can lift 10-pound weights and write his name, they reported. He has sensation in all five fingers. He also can move his shoulder and elbow although he does not have full extension. The boy currently is wearing a splint until further surgical procedures are carried out some time in the near future.

The other patient, whose right arm was severed just above the elbow in 1963, is now working full-time as a machinists' supervisor, according to the report. Strength is increasing in the fingers and movement of the shoulder is only somewhat restricted. However, no independent movement of the elbow is possible. Further reconstruction procedures also are planned for this patient.

Replantation of a totally amputated extremity is largely the applied synthesis of existing knowledge, the surgeons commented. By 1944 the surgeon's attitude and skill were "unquestionably adequate," they said, although replantation was not performed in two major wars. Replantation became an established laboratory procedure in the present decade, and well-trained surgeons repaired combinations of injuries of the extremities so severe that attempts to distinguish the degree of separation of a limb were "mostly matters of semantics," they pointed out.

Although the trained surgeon has the ability to perform a successful arm replantation, the authors warned that the magnitude of the subsequently required reconstruction procedures means that the hospital must have the resources to provide the patient better function than he could achieve with a good artificial arm.

If the hospital has the necessary facilities, they said, "we believe that indications for replantation currently exist in the actively productive person with a severed arm, no detectable injury to vital internal organs, no urgent problem with respect to the other arm, and a positive desire for his own limb at the expense of unpredictable periods of hospitalization and unpredictable end result.

"With advances in surgical science, the indications will undoubtedly be broadened."

The authors are affiliated with Massachusetts General Hospital and Harvard Medical School.

Cholesterol Import Limited In Artery Disease

A study of 1,700 patients with hardening of the arteries revealed no definite correlation between the level of cholesterol in the blood and the nature and extent of their disease, a Baylor University research team reported today.

Eight out of 10 patients, or 78 per cent, had cholesterol levels within the normal range for Americans, according to the report in the current Journal of the American Medical Association.

The values for patients with widespread atherosclerotic disease were not remarkably different from those among patients whose disease was more limited, H. Edward Garrett, M.D., Evan C. Horning, Ph.D., Billy G. Creech, Ph.D., and Michael De Bakey, M.D., Houston, wrote in the Journal.

Furthermore, there was no marked difference in cholesterol values between patients with occlusive disease in which arteries become blocked and those with aneurysmal disease in which arteries develop bulges, they said.

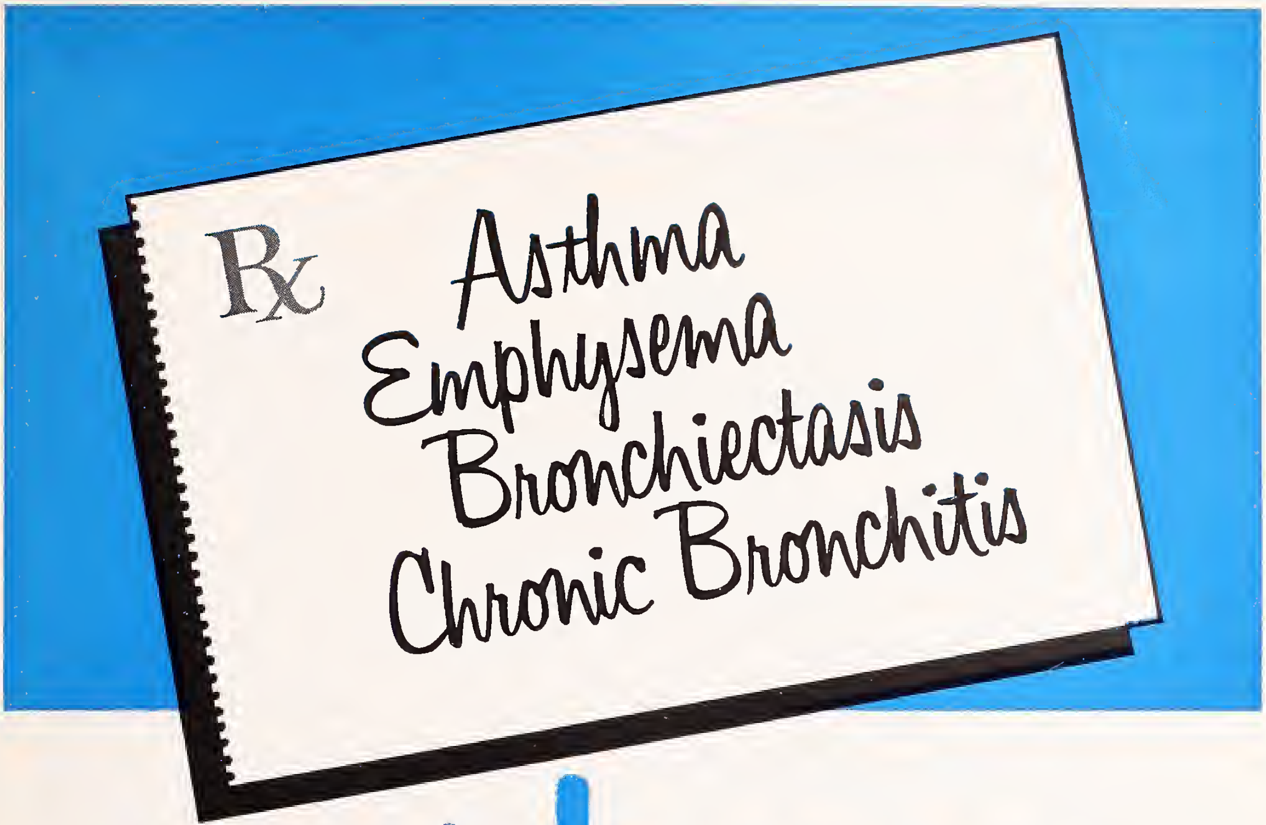
The study group included 1,416 men and 284 women, ranging in age from 20 to 85. Fifty-six per cent had occlusive disease and 44 per cent had aneurysmal disease. All patients required surgery and in this sense the degree of atherosclerosis was severe in all cases, it was pointed out.

Additional cholesterol determinations were made for 200 of the patients for comparison with healthy men in Finland, Finnish men with coronary artery disease, and a group of healthy Minnesota business and professional men. Cholesterol values of the Houston patients were generally higher than those for the healthy Minnesotans, but were lower than those in the Finnish coronary group, and not very different from those of the normal Finns.

"These observations support the judgment that, at best, the basal cholesterol level in an individual patient is a valid predictive factor as regards the presence and extent of atherosclerotic disease only when placed in relation to other and perhaps more consequential factors," the authors concluded.

In populations relatively free of atherosclerotic disease, blood cholesterol values are usually low and are well below the average values found among Americans who have "an alarming degree" of atherosclerosis, they commented. From these studies, they said, it has been concluded that cholesterol level, as an index of altered fat metabolism, may be related to the incidence of the disease in various populations. Current efforts at reduction and control of blood cholesterol levels by means of diet or drugs, or both, are based on this concept, they added.

However, the researchers said, their investigation suggested that studies which focus on blood cholesterol levels to the exclusion of other possible determinants of hardening of the arteries carry "only the remote likelihood of contributing additionally or significantly to solution of the problem" of the causes of this disease.



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DIABETES WEEK

November 15-21

Dr. Cecil Striker, Associate Clinical Professor of Medicine, University of Cincinnati College of Medicine, will inaugurate DIABETES WEEK in Connecticut and address a joint meeting of the Connecticut Diabetes Association and the New Haven Medical Association at the Medical Society's auditorium, 364 Whitney Avenue, Wednesday, November 18, 1964 at 8:30 p.m.

Dr. Striker was the first President and Founder of the American Diabetes Association.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

A Marriage Manual For Catholics. By William A. Lynch, M.D., Triden Press, New York, 1964. With a Foreword by his Eminence Richard Cardinal Cushing, 346 pp., $4.95.

New Dimensions In Psychosomatic Medicine. Edited by Charles William Wahl, M.D. with 13 authors, Little, Brown & Co., Boston, Mass., 1964, 334 pp., $8.50.

Diseases Of The Heart And Blood Vessels, Sixth Edition. Nomenclature and Criteria for Diagnosis by The Criteria Committee of the New York Heart Assoc., Little, Brown & Co., Boston, Mass., 440 pp., Illustrated, $5.50.

Infectious Diseases of Children, Third Edition. By Saul Krugman, M.D., and Robert Ward, M.D., The C. V. Mosby Co., St. Louis, Missouri, 1964, with 66 figures, 8 plates in full color, including a gatefold insert, 403 pp., $15.75.

Proceedings Of The World Forum On Syphilis And Other Treponematoses. Washington, D.C., September 4-8, 1962. A public Health Service publication of the U.S. Dept. of Health, Education, and Welfare. Sponsors: American Social Health Assoc., American Venereal Disease Assoc., U.S. Dept. of Health, Education, and Welfare, Public Health Service, 508 pp. $4.00.

A Mission In Action, The History Of The Regional Hospital Plan Of New York University. By Clarence E. De La Chapelle, M.D. and Frode Jensen, M.D., New York University Press, 1964, 45 pp. $4.00.

Textbook of Pediatrics, 8th Edition. Edited by Waldo E. Nelson, M.D., D.Sc., With the Collaboration of Eighty-Five Contributors, W. B. Saunders Co., Philadelphia and London, 1964, 1636 pp., Illustrated. $18.00.

Foetal And Neonatal Pathology, Second Edition. By J. Edgar Morrison, M.D., D.Sc., Butterworth, Inc., Washington, D. C., December 1963, 552 pp., Illustrated. $19.50.

Cellular Injury. Ciba Foundation Symposium. Edited by A. V. S. de Reuck, M.Sc., D.I.C., A.R.C.S. and Julie Knight, B.A., Little, Brown and Co., Boston, 1964, with 81 illustrations, 403 pp. $12.00.

Animal Behaviour and Drug Action. Ciba Foundation Symposium Jointly with the Coordinating Committee for Symposia on Drug Action. Edited by Hannah Steinberg, Ph.D. for Coordinating Committee; and A. V. S. de Reuck, M.Sc., D.I.C. and Julie Knight, B.A. for Ciba Foundation, Little, Brown and Co., Boston, 1964, with 103 illustrations, 491 pp., $13.00.

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Connecticut Medicine

Connecticut State
Medical Journal

Volume 28 / December 1964 / Number 12

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"THE HOPKINS" AND MEDICAL EDUCATION (see page 849)

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Dosage: Doses should be individualized for each patient. The usual adult sedative dosage ranges from 30 mg. (1/2 grain) to 50 mg. (3/4 grain) two or three times daily.

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Connecticut Medicine

editorials

Basic Science And Practical Medicine: Problems In Cardiac Pacing

When a patient's life is in jeopardy by the threat of cardiac standstill as is so common in Stokes-Adams disease, the accepted procedure is first to introduce an intracardiac pacemaker, by catheterization of the right ventricular cavity to pace the heart while an external pacemaker is implanted on the ventricular surface. But this obviously life-saving and innocuous procedure raises a number of important questions. One is whether there is an optimum location for the implantation of the pacemaker or whether its application anywhere on the left ventricle is sufficient. Another is what to do when the implanted pacemaker begins to fail.

It has been known for a long time that a ventricular contraction initiated from either the right or left lateral ventricle gives rise to a beat which is quite inefficient. First, one ventricle is activated, much later the other is activated and the resulting systole is comparable with what one finds in ventricular ectopic beats during which the ventricular muscles do not contract coordinately, and therefore the ventricle does not empty efficiently. The circulation can be maintained to be sure but the cardiac reserve goes down. On the other hand, if the stimulus is applied to the anterior septum, both the right and left ventricles contract more or less simultaneously and empty more efficiently, A glance at the electrocardiographic complexes found in many patients with cardiac pacing reveals that all of them are of the left bundle branch block type indicating that the cardiac surgeons have not implanted the pacemaker in the optimum location. Attention to this simple physiologic fact should assist a paced heart to perform more efficiently.

The other question is what to do when the implanted pacemaker begins to fail. Long-term experience with implanted pacemakers reveals that the most common cause for cessation of pacing was a mechanical break in the electrode leads. Other causes include failure of electronic components, and mechanical separation of the electrode from the heart.[1] This mechanical separation is caused by fibrin deposition around the electrode and is promoted by the constant friction occasioned by contraction and relaxation of the ventricle. In consequence, the threshold for an effective stimulus is raised. If an increased stimulus cannot be delivered, then at the first rise in threshold the heart will respond only if the stimulus falls during the supernormal period of an idioventricular beat. The supernormal period extends from the downstroke of the T wave until after the summit of the U wave.[2] In fact, a response only during the supernormal period is a telltale sign of a failing pacemaker stimulus.

Battery exhaustion, when not related to penetration of the pacemaker by physiologic fluids, is infrequent. However, a characteristic of mercury batteries, which are invariably used as power sources, is that voltage drops precipitously at the end of battery life. Consequently, if one can temporize by means that can reduce the myocardial threshold, even though the success is likely to be brief, it can give a respite to the threatened patient until a replacement can be made.

THE COVER

"THE HOPKINS" AND MEDICAL EDUCATION

SUCCESS of The Johns Hopkins University School of Medicine, opened in Baltimore, Maryland, in 1893, stemmed from policies developed at meetings of the Faculty of Medicine and its advisors during formative years. The School, with cooperation of The Johns Hopkins Hospital, was to become world renowned for emphasis on research, for high admission standards, and for innovations in medical training. These advanced teaching methods influenced a revolution in medical education, led to higher requirements for medical licensure, brought about closure of many substandard schools of medicine and helped raise the status of medicine in the United States to a position of true world leadership.

We have known for a long time that potassium depletion decreases responsiveness to an implanted pacemaker. In such a circumstance this could be an additional cause of pacemaker failure. In fact, such a patient was described by Leon-Sotomayor, et al. in 1962.[3] The opposite is also true as was demonstrated by Siebens et al.[4] He showed a parellel increase of myocardial responsiveness by increasing the serum potassium levels from three to nine m.eq. per liter. In their experiments an increase of serum potassium from three to six m.eq. per liter reduced the required stimulus to reach threshold by approximately 40 per cent.

Walker, Elkins and Wood[5] also demonstrated in two patients with implanted pacemakers that responsiveness to a pacemaker can be increased by potassium administration even in the presence of normal serum potassium levels. They point out that if the pacemaker's malfunction results only in a response during the supernormal period of an idioventricular complex, that then the problem is that the pacemaker is now capable of delivering only a subthreshold stimulus. Obviously the threshold to the stimulus must be quickly lowered as they did with administration of potassium and one must immediately prepare for a replacement of the failing pacemaker.

The probable mechanism by which potassium increases myocardial excitability is through decreasing the transmembrane resting potential of the myocardial cell. If at the same time there is no change in the threshold potential of the cell, then a smaller electrical charge would be required to depolarize the membrane and cause contraction of the myocardial fiber. This mechanism has been suggested by Hoffman and Cranefield[6] to explain the supernormal period of excitability: a combination of a slightly reduced transmembrane potential with an unchanged threshold potential that results from excitability being restored before the fiber is fully polarized.

When Nahum and Hoff[2] studied the supernormal period of excitation in dog and chimpanzee hearts, they pointed out the importance of this period of lowered threshold in the genesis of abnormal ventricular rhythms. However, Nahum and his associates did not find a supernormal period in normal dogs, nor did Feldman[7] in human hearts. It may very well be that normal hearts, not injured either by an implanted electrode or other pathologic processes do not exhibit a supernormal period. However, in damaged hearts, the supernormal period exists and is reproducible as Walker showed in his two patients, and as Nahum and Hoff described its existence in a chimpanzee heart with an implanted electrode. So did Linenthal and Zoll[8] report a supernormal period of excitability in seven human hearts and implanted pacemakers. It is knowledge of the meaning of the supernormal period and the action of the potassium ion on the threshold of excitation in the ventricular muscle which made possible the studies by Walker et. al.

Walker, Elkins and Wood's study of two patients with a failing pacemaker is a model of clinical investigation. They knew of the meaning of the supernormal period, from a knowledge obtained from basic science investigation. They knew also of the effect of the potassium ion upon the threshold of myocardial excitability; low serum potassium increases it and high serum potassium lowers it. They tried lowering the serum potassium and almost stopped the heart. They then raised the serum potassium and rendered the heart more responsive to a subthreshold stimulus. In fact, they went searching for other substances that might also do what the potassium ion did, but neither isoproterenol, calcium, nor hydrocortisone could do it. In their work, we see again the indissoluble bond between basic science and practical medicine.

L.H.N.

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Science Tools:
16. Gold Plating In Surgery

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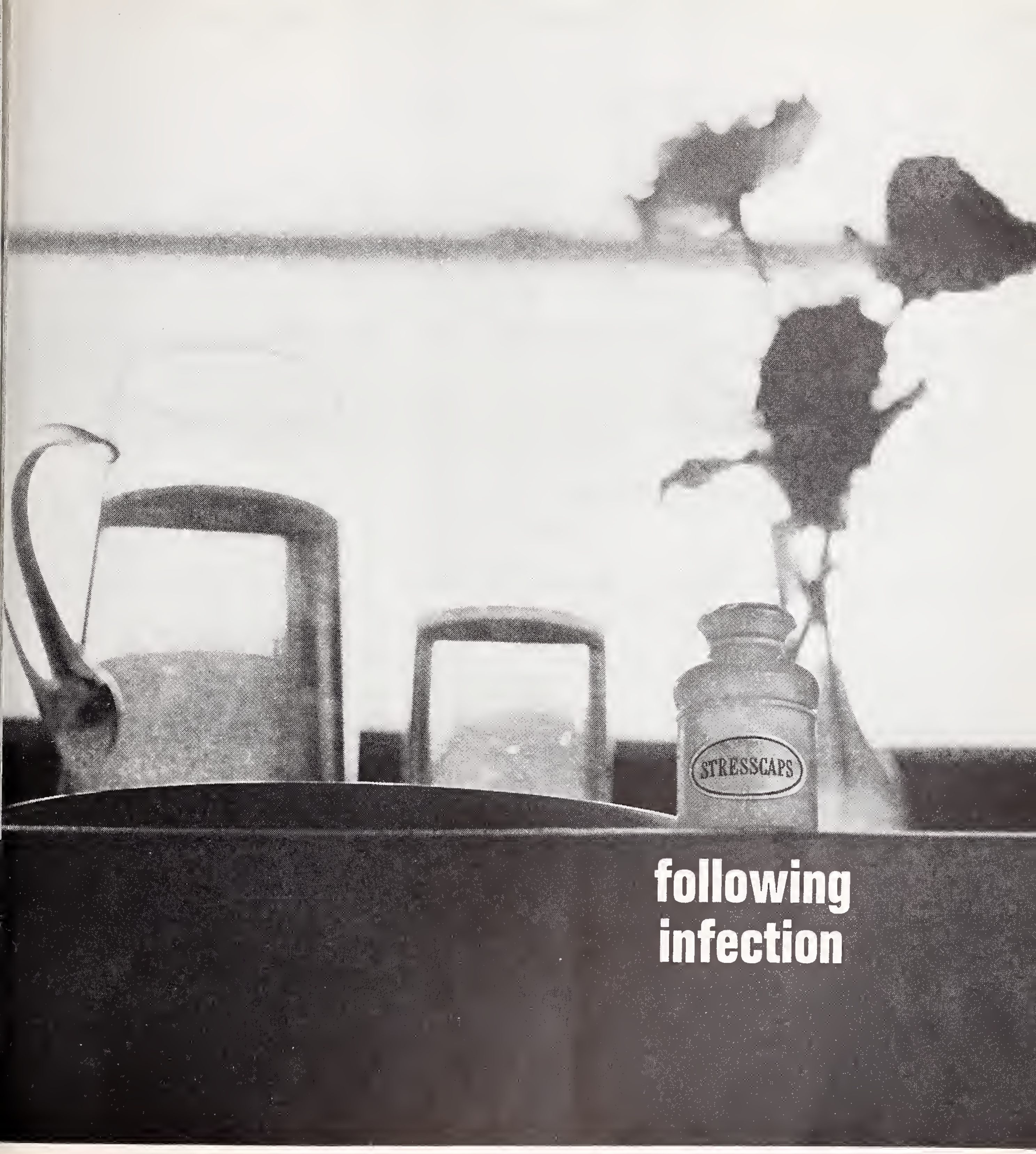

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to withstand aortic pressure in the rabbit aorta between 90-150 mm. mercury without losing its adherence to the vessel wall.[1]

An electrostatic charge is conferred on gold leaf merely by stroking a camel's hair brush against a rubber comb and then touching the leaf with the charged brush. Accepting the electric charge and sticking to the brush, the gold leaf can be placed directly on the site of hemorrhage, lacerated or sutured artery or any other surgical target. When the charged leaf is touched to the tissue surface, it is released immediately from the brush and clings tightly to the tissue surface. The strength of adherence between the gold leaf and vessel wall depends on the amount of electrostatic charge conferred on the leaf. Apparently, living tissue has a negative charge and this is why a positively charged gold leaf adheres to it so firmly. Once it is laid on tissue, further light stroking with the camel's hair brush will cause the leaf to clutch the structure even more tightly and remain there permanently.

The permanent arrest of hemorrhage from arteries and veins and oozing capillary beds has posed a serious problem for generations of surgeons. In the first place, it is often not feasible to control bleeding by ligating large vessels anywhere especially in a vital organ like the brain, or heart. In the second place, ligating even small vessels may be fraught with serious danger. For these reasons it is customary to arrest hemorrhage by tamponading the bleeding site with tabs of muscle, gauze packs or by applying substances such as vaso-constrictor drugs. Except when the vessel has been ligated, the hemostatic effect after use of all other methods depends on the formation of a thrombus in the hole in the vessel wall. If the circulation through the vessel is sluggish or if other conditions exist which favor thrombosis, the mural thrombus plugging the hole in the vessel may soon fill the entire lumen and close it off just as completely as if it had been ligated.

The laboratory studies of Gallagher and Geschickter on the use of gold leaf in surgery are classic examples of the investigation in animals and then applying the knowledge obtained in human patients. They performed twenty-one experiments on rabbits and found charged gold leaf to be effective in arresting hemorrhage from puncture wounds of the largest vessels in the body; the aorta and inferior vena cava. They demonstrated that gold leaf was highly effective in arresting hemorrhage of capillary origin. The hemostatic effect was prompt and enduring as shown by autopsy examination of these animals as late as ninety days after the vascular surgery. Neither thrombosis, loss of patency nor reactive fibrosis occurred. Instead, the gold leaf served as a non-irritating binding mesh for regeneration of endothelial lining, connective tissue or capillaries, and no post-operative hemorrhage was found from any of the experimental vascular wounds.

Such experiments made it clear that charged gold leaf could serve a similar purpose in clinical surgery. In humans, the authors used the leaf to stop capillary, arterial, and venous bleeding of dura mater, cerebral and cerebellar cortex, spinal cord, periosteum, muscles and ligaments. They encountered no adverse tissue reactions and healing in all cases has been by primary intention. It was necessary, however, to use gold leaf that was two to three times the thickness of the ordinary commercial leaf to furnish enough tension to stop an arterial jet. It is also necessary to use wooden rather than metal instruments to handle the gold leaf. After the leaf has been applied to the vessel wall, brushing it will cause firmer adherance but the stroking should not be vigorous enough to break the gold leaf. The surface did not need to be dry but the leaf had to be placed directly on the hole in the vessel.

Gallagher and Geschickter point out that the method can be used as a protective covering on all surgical suturing and in gastrointestinal operations to cover anastomoses and to prevent adhesions. It would appear that with so much vascular repair going on at the present time, much time might be saved, by reducing the number of sutures and supporting the vessel with gold leaf. Doubtless surgeons in other areas will soon find uses for this excellent material. The adherence, malleability, chemical inertness and tensile strength of gold leaf will be of singular value in surgery.

Although gold leaf has not hitherto been employed to any extent in surgery, gold foil was used by Unger in 1947[2] to close a perforated ear drum in suppurative otitis media. Gold itself has long been used. Imbert and Moiroud[3] reported a patient in whom a perforated gold plate had been used to cover a large defect in the cranium and after forty years it was still in place without any sign of adverse tissue reaction. Other metals, however, such as silver and tin produced severe reactions when implanted in the brain of a cat.[4] Gold, because of its chemical inertness, appears to be ideal for use in human tissues. What was needed was knowledge of the physical properties of the rubber comb, the camel's hair brush and the noble metal — gold, knowledge of the electrical charge of living tissues, and an insight by the investigator. When all these were put together, we have arrived at a first-rate contribution to clinical surgery.

L.H.N.

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Science And Counterfeit Science

How does one discriminate between the true scientist and counterfeit science. Of course, it is argued that the crackpot can be spotted by the way he tries to communicate. If he talks like a crackpot, fine, perhaps he can be so damned, but there is a risk involved in doing so. Many weird ideas have been advanced in the form of true science, and there are also many examples in history of people we now regard as outstanding scientists whose early writings look like those of a raving maniac.

For every article one sees in a technical journal or for that matter, in the public press, a decision has to be made. Is it worth reading or is it something that can safely be skipped. Of course, in a learned journal, the problem of an article is made easier for the reader because the editor has already carefully scrutinized the contribution and rejected it if it seems to have come from a crackpot. Nevertheless, there is really no acid test or even a small group of tests that serve to distinguish between crackpot work and good science. For this reason Gruenberger has offered a check list of some of the attributes of science and of the crackpot to help in making this decision.

Three items seem to be of significant value. Public verifiability, predictability and controlled experimentation. The scientist says–I did this and so—and you are free to repeat the steps. The crackpot says—There is revealed truth and I and my followers can obtain the results. How reminiscent of all the cancer cures (twelve points).

Predictability (12 points), is whether what the scientist discovers is applicable to the future. When a man can predict and the predictions turn out to be true as in the case of Einstein for example, a great deal has been gained toward credibility. The honest scientist will usually admit those of his predictions that did not work.

Controlled experiments (13 points), rank high on the list of distinguishing between science and fantasy. The scientist seeks to devise controlled experiments whereas the crackpot seeks to avoid them or if some are performed and they didn't work out, he is always ready with a marvellous excuse to explain why they did not bear out his theories.

Fruitfulness (10 points), is the ability to suggest new ideas. While an important attribute of science, it is itself a poor discrimination between the scientist and the crackpot since the latter is always filled with new ideas though they are not working hypotheses that can be experimentally useful.

Authority (10 points), is another valuable weight. It tells among scientists. Each new subject is supposed immediately to be submitted to known and recognized scientists for both opinion and test. If the answer is "nonsense," it does count although authorities may be wrong and have been many times in the past. Mostly they are however reliable. Can we imagaine a crackpot seeking opinions from a recognized authority?

Ability to communicate (8 points), is next in importance in the "box score." Most scientists discipline themselves in accepted methods, language symbols, to present their work to their colleagues or editors. The crackpot scorns such means of "knuckling under" to accepted practices.

Then come in lesser order of weight to the box score several items. Occams razor, humility, open-mindedness, Fulton non-sequitur, Paranoia, the dollar complex, and statistic compulsion.

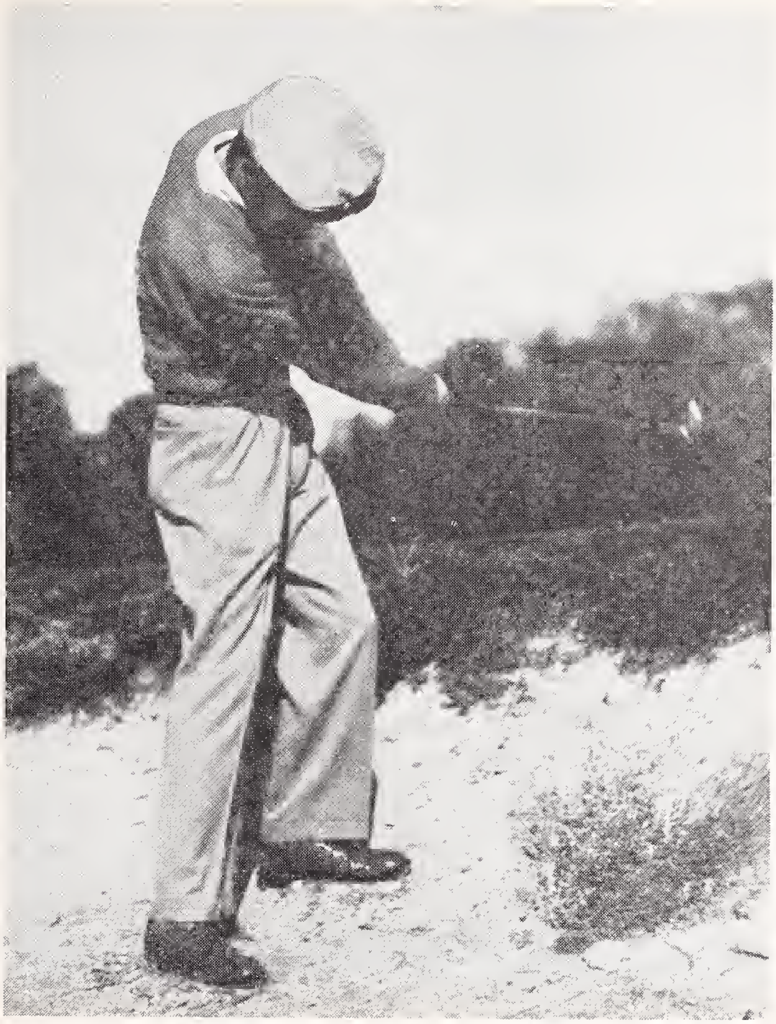
Occams razor (5 points), is a principle which says that of two possible explanations for the same phenomenon, scientists prefer the simpler one that requires the fewest hypotheses. A simple hypothesis which explains everything is that the devil deliberately makes what appears to be patterns to deceive us, but there is no pattern. Occams razor applied to Copernicus, who advanced a much simpler explanation for planetary motion than the one invoked by his contemporaries. In the absence of contrary evidence, the scientist is inclined to accept the simpler explanation.

Little need be said about *humility* (5 points). To be sure, there have been arrogant scientists but we tend to honor the humble ones. Few if any crackpots have ever been guilty of humility.

Open-mindedness (5 points), is in general not a good discriminator. Many true scientists have been stubborn, but he uses language like "it appears that," "It would seem plausible." You can recognize the crackpot because he is dogmatic, arbitrary, and you must either agree with him or "lie forever beyond the pale."

The *Fulton non-sequitur* (5 points), is a negative test. It is often however enough to spot a crackpot on this test alone. He proceeds with the argument "They laughed at Fulton. He was right. They're laughing at me. Therefore, I must be an equal genius." This is so obvious, but it keeps recurring.

Paranoia (5 points), is also a negative test. A crackpot can be spotted on this test alone. He feels the world deliberately hates him, actively opposes



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rational combination therapy for sprains and strains: relaxes muscle, relieves pain. Also available with ¼ gr. codeine as 'SOMA' COMPOUND with CODEINE: carisoprodol 200 mg., acetophenetidin 160 mg., caffeine 32 mg., codeine phosphate 16 mg. (Warning: may be habit-forming.)

BRIEF SUMMARY
'SOMA' COMPOUND; 'SOMA' COMPOUND plus CODEINE: carisoprodol, acetophenetidin, caffeine, codeine phosphate. *Warning: Codeine may be habit-forming.* **Indications:** 'Soma' Compound and 'Soma' Compound with Codeine are indicated for relief of pain and stiffness in traumatic, rheumatic and other similar conditions. **Contraindications:** Allergic or idiosyncratic reactions to carisoprodol or codeine. **Precautions:** *Acetophenetidin*—May damage the kidneys when used in large amounts or for long periods. *Codeine*—Should be used with caution in addiction-prone individuals. *Carisoprodol*—Like other central nervous system depressants, should be used with caution in patients with known propensity for taking excessive quantities of drugs and in patients with known sensitivity to compounds of similar chemical structure, e.g., meprobamate. **Side effects:** *Codeine*—Nausea, vomiting, constipation, and miosis. *Carisoprodol*—The only side effect reported with any frequency is drowsiness, usually on higher than recommended doses. One instance each of pancytopenia and leukopenia occurring when carisoprodol was administered with other drugs has been reported as has an instance of fixed drug eruption with carisoprodol and subsequent cross-reaction to meprobamate. Rare allergic reactions, usually mild, have included one case each of anaphylactoid reaction with mild shock and angioneurotic edema with respiratory difficulty, both reversed with appropriate therapy. Other rarely observed reactions have included dizziness, ataxia, agitation, increase in eosinophil count, and gastrointestinal symptoms. Massive overdosage may produce coma and/or mild shock and respiratory depression. **Dosage:** 'Soma' Compound and 'Soma' Compound with Codeine, one or two tablets three times daily and at bedtime. **Supplied:** 'Soma' Compound, orange tablets, each containing carisoprodol 200 mg., acetophenetidin 160 mg., and caffeine 32 mg. 'Soma' Compound with Codeine, white, lozenge-shaped tablets, each containing carisoprodol 200 mg., acetophenetidin 160 mg., caffeine 32 mg., and codeine phosphate 16 mg. Narcotic order form required. *Before prescribing, consult package circular.*

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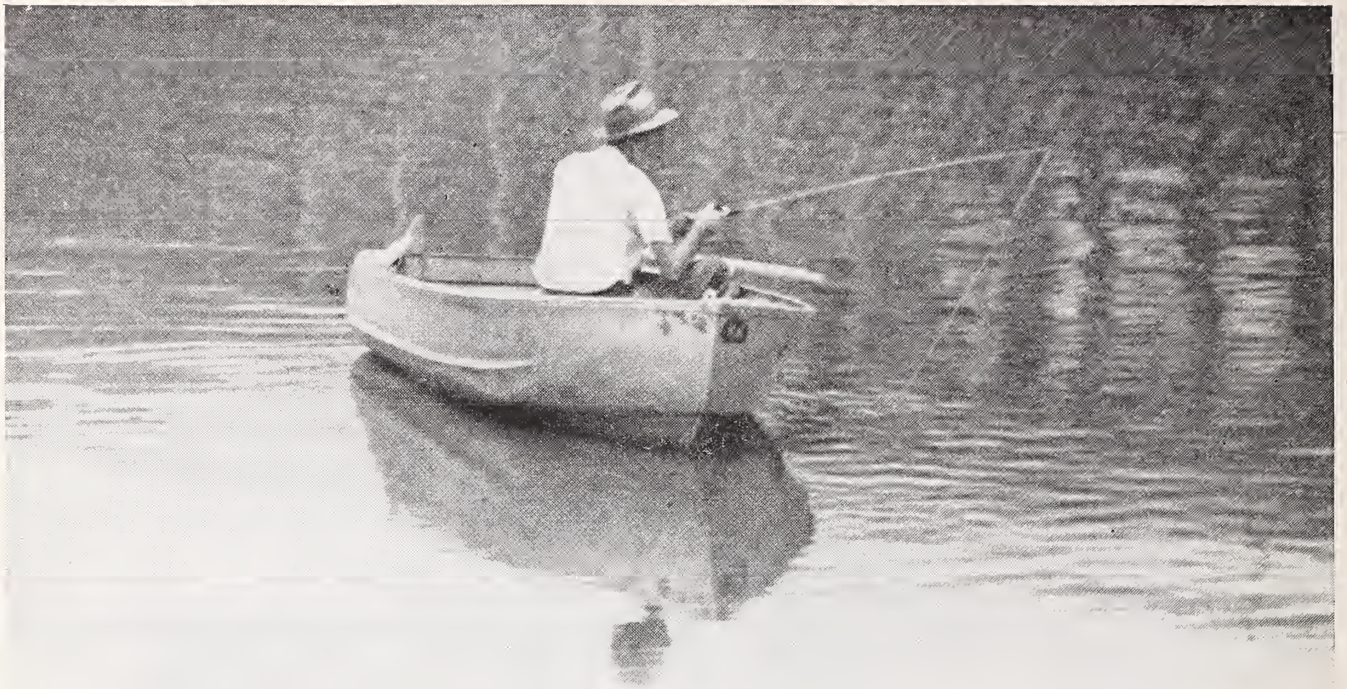

The discharged
mental patient . . .
and Thorazine®
brand of chlorpromazine

"The average practitioner is quite capable of handling the vast majority of ex-institutionalized patients by regulation of medication, reassurance, manipulation of the environment where necessary, and . . . other technics." Kline, N.S.: Postgrad. Med. 27:620 (May) 1960.

The family physician must often assume responsibility for the discharged mental patient. Thorazine (chlorpromazine, SK&F) can be a valuable adjunct to the continuing care of this patient, because it helps prevent relapses by insulating him from the impact of stressful experiences. For successful rehabilitation and prevention of rehospitalization, however, the former mental patient—and often his family—also needs the guidance and counsel of his physician.

Many physicians are surprised by the high doses of Thorazine (chlorpromazine, SK&F) used in patients released to their care from mental hospitals. This surprise may be expressed by a drastic reduction in dosage "to play it safe"—with serious consequences for the patient.

The successful maintenance of former mental patients requires adequate, often "high" dosage, and often for prolonged periods of time. Fortunately, these dosages do not mean greater risks for the patient. On the contrary, there is much less risk of serious side effects once a patient has become gradually accustomed to Thorazine (chlorpromazine, SK&F)—*regardless of dosage*—over a period of a few months. Continuing therapy is almost always well tolerated, and is essential to most patients' continued well-being.

Brief Summary: Thorazine (chlorpromazine, SK&F) has been successfully used for 10 years in the treatment of mental and emotional disturbances, and has proven highly effective in the maintenance therapy of former hospitalized mental patients. *Principal side effects:* The most frequently encountered side effect is transitory drowsiness. Other occasional side effects include: dry mouth, nasal congestion, constipation, miosis, dermatological reactions, photosensitivity, jaundice, hypotension, increased appetite and weight; very rarely, mydriasis, agranulocytosis, extrapyramidal symptoms. *Contraindications:* Comatose states or in the presence of excessive amounts of C.N.S. depressants.

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his project. To him this opposition itself is good enough cause for the truth of his project.

The *dollar complex* (5 points), is also a negative test. The crackpot almost always is overly impressed with the value of his discoveries—they're earth-shaking. The true scientist will never say that his discovery "is truly revolutionary."

The last and least contribution to the box-score between scientist and crackpot is *Statistic compulsion* (5 points). It seems to be a characteristic of crackpot literature that statistics are not only used but continuously explained. A coin tossed one-thousand times does not necessarily fall heads five-hundred times—it may fall five-hundred and twenty-three times heads. "Therefore, beware of statistics." The scientist who knows his statistics generally assumes that his reader is informed and never uses an exclamation point to end a sentence.

The reader is now asked to apply the check list to any scientist, nostrum, black magic, shark's teeth, snake oil, cancer cure, political panacea and what have you. They will all rate very low scores. The charlatan and the boob are both intrisically opposed to the search for truth. The last thing they want is verifiability and controlled experimentation. In fact, when we insist on such tests and the results fail to support the claims, the non-scientist calls in a marvelous array of excuses as to why the "uninitiated" have perverted his domain.

Gruenberger points out that things are not all black. He analyzes extra-sensory perception (ESP) and finds a complete lack of open-mindedness. Using Occams razor he finds a marvelously simple explanation for all wonders of ESP. Namely, they don't exist or that simple natural explanations are at hand.

Let us each apply Gruenberger's box score on other fads and see how they come out.

L.H.N.

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Gruenberger, F. J.: A Measure for Crackpots, Science 145, 1414, Sept. 25, 1964.

Pharmacogenetics— A New Discipline

We have known for a long time that unsuspected differences among men come to light when they are challenged by certain drugs. What the cause of these differences may be is now coming to light as a result of progress in cellular and molecular biology and physiology which has begun to reveal that these differences are really the result of hereditary variations. In consequence, a new discipline is evolving in medicine termed pharmacogenetics. It may be expected that it should help the physician in choosing the right drug and in the proper dosage for each individual and help to define more sharply the limits of safety and effectiveness of many drugs both new and old.

This has all developed from the work of G. Beadle and E. I. Tatum (Nobel prize winners in 1958) on mutations produced in a mold by X-rays. They concluded that each gene may be responsible for the specific nature of a simple enzyme. When the gene is functioning normally, then the enzyme which it controls operates efficiently. If the gene is damaged, the activity of the enzyme will be impaired or destroyed.

One instance of how a genetically impaired enzyme may affect the individual's response to drugs came to light when two members of a family developed severe anemia after treatment with sulphonamide drugs. These two members were found to have red cells whose mean life time was very short even in the absence of drugs and when they were given sulfonamides this reduced the brief life span of the red cells even further. It turned out that these two members had two kinds of hemoglobin, hemoglobin A which is the usual type and another, a hitherto unknown type subsequently called hemoglobin Zurich. By electrophoretic studies it was discovered that the hemoglobin Zurich has an amino acid arginine, in place of histidine in one of the two polypeptide chains present in the globin fraction of the hemoglobin molecule.

Genetic studies of the two patients revealed fifteen members whose red blood cells contained hemoglobin Zurich and among them were some with a history of anemia. Both males and females were affected and all affected individuals studied were heterozygous having both hemoglobin A and hemoglobin Zurich. This characteristic is inherited as a non-sex linked dominant character. In such deviations each allele—a gene consists of two alleles, one from each parent—specifies a different protein. The anomaly is harmless unless the red blood cells are challenged by sulfonamides or related compounds.[1]

There is now a growing list of genetically determined conditions in which the variation is attributable either to a reduction in enzyme activity or an excess. When there is a reduction, the enzyme molecule may be less well fitted for activity than it normally would be or the genetic variation may be such that no enzyme is made or there may be some change in the regulatory mechanism which controls the quantity of the enzyme produced. We now know several of these genetically determined conditions associated with a reduction in enzyme activity and a greater susceptibility to the toxic effects of drugs. One of these, a deficiency of glucose–six phosphate dehydrogenase is a sex-linked characteristic and carries with it an increased susceptibility to such drugs as quinine, phenacetin and aspirin.

Dr. D. A. P. Evans of the University of Liverpool, England, told a recent Academy Conference on Evaluation and Mechanism of Drug Toxicity, how another genetic variant was discovered when the metabolism of isoniazid came under study. This drug, important in the treatment of tuberculosis, produces nerve damage in some patients.[3] Six hours after isoniazid was given to two hundred and seven people in fifty-three families, Dr. Evans measured the concentration of the drug in the blood. He discovered two groups. One had about one unit in the blood, the other nearer five units. By a series of ingenious experiments and astute deductions, he found that those individuals with small amounts of isoniazid were rapid inactivators by acetylating the drug. While those with large amounts of isoniazid were "slow inactivators," since they acetylated the drug very slowly. The enzyme responsible for inactivation, acetyl transferase, is found in the liver and the "slow inactivators" have too little of it. It is among the slow inactivators that we find occurrence of drug toxicity and peripheral neuropathy when given isoniazid.

Slow inactivators of isoniazid were found by a microbiologic technique in about half of the white American population but in only ten per cent of the Japanese population. There are few among the Chinese, while the Sudanese show a very high percentage of slow inactivators. Why the Asiatics show so few "slow activators" is not known.

There are also some individuals who possess too much of a certain enzyme. Generally human genetic variants respond to drugs with toxic manifestation due to reduced enzyme action. There is one notable exception. It has been known for a long time that some people who have taken quite ordinary amounts of some drugs like the barbiturates and others, develop severe abdominal pain often associated with symptoms referable to the nervous system. This toxic reaction may even be fatal. Other members of the same family show unusual sensitivity to light and may develop skin disorders. These unusual manifestations are associated with the excretion of a large amount of some of the precursors of porphyrin, a substance which the bone marrow uses to build the heme part of the hemoglobin molecule. The condition is known as hepatic porphyria. Dr. Granlick of the Rockefeller Institute told the conference that in these cases, the liver "goes berserk" and manufacturs the enzyme epsilon aminolevulinic acid synthetase at an alarming rate. This enzyme in turn starts a chain reaction which leads to the building of porphyrin precursors at a rate out of proportion to the need of the individual. The potentiality of a drug to cause porphyria, Dr. Granlick said can be discovered by its action on the liver cells from chick embryos.

The use of animals for the analysis of genetic influences on drug toxicity has just begun. Already strains have been developed which analogous to known human strains in terms of drug response. For example, there are strains of mice that differ in response to chloropromazine which as we all know is widely used in mental illness. In a paper on pharmacogenetics which won an A. Cressy Morrison award from the New York Academy of Sciences in 1963, Doctors G. B. West and J. M. Harris of England reported the development of strains of rats which varied in their allergic response to egg white and dextrin. Since egg white allergy in man is also inherited, we shall soon learn much about the cause of drug reactions in man of an allergic nature.

L.H.N.

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Pathologic Malingering

"And if a man is not lame, blind, or halting, and he feigns to be one of these, he will not die in his old age before he actually becomes as one of these."
—Talmud, Mishnah Peah VIII: *9*

The idea of making gain out of feigning disability is an old one. Shaw[1] quotes Rabbi Folkman who observed that it was already recognized in Judea in the middle of the second century B.C. by Rabbis who discovered people taking unwarranted advantage of relief facilities made available by the Biblical legislation in Leviticus 19:15. People feigned disability to exploit the generosity of farmers who followed the Biblical law. It is interesting that the Rabbis accepted such "illnesses" as real and interpreted it as a divinely appointed punishment. Thus the ancient code supports the belief in the reality of the pain in the extremity of a "pathologic malingerer." In these columns we have previously called attention to the difference between pain and suffering, pointing out the psychological element of the elaboration in the central nervous system of the purely physical nature of impulses ascending the peripheral nerves.

Shaw, from a study of an increasing flow of patients during the past twelve years both in the peripheral vascular laboratory of the Massachusetts General Hospital and private practice, has at-

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* AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181:411-423 (August 4, 1962).
AMA Council on Foods and Nutrition: Composition of Certain Margarines, *JAMA* 179:719 (March 3, 1962).

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tempted to define some of the clinical characteristics of the pathologic (motivational) malingerer, the patient who maintains disability of an injured extremity for unadmitted gainful purposes. From the history we find a complaint of disabling pain after an extremity injury, but persisting well beyond the time ordinarily required for wound healing. There is generally an unsettled law suit as well as an inadequacy or unhappiness in work, school or home.

The physical examination shows the patient as hostile or defensive. They are ready to accept rehabilitation but must first be relieved of the pain. The involved extremity is protected and held motionless, the function is painful and lost in varying degree. The hand can't grasp, the foot can't bear weight. Voluntary movements are prevented by opposing muscles and passive movement is resisted by cries of pain. The pain is not imaginary but real since the limb shows secondary effects of long immobilization in the form of coldness, cyanosis, edema, muscle atrophy, sweating and incompletely desquamated skin. Light touch causes as much pain as deep pressure or movement and tenderness is maximal at the point of original injury. Sympathetic nerve block restores warmth in the extremity, so also does placebo block with saline. Any treatment that tends to face the patient away from his disability makes the pain worse. Hence, active physiotherapy aggravates but immobilization in a plaster cast relieves. At the same time there is no evidence of an unhealed anatomic lesion to account for the symptoms.

Shaw has classified his patients into three groups: The first consists of those motivated towards complete recovery but who were forced by injury to suffer extremity immobilization and symptoms resulting from disuse. These quickly recover. A second group comprise the "unmotivated," those who care little either about getting rid of or perpetuating their disability. This group is not hostile and when subjected to conscientious, active physiotherapy will secure an excellent result.

The third group consists of patients who are positively motivated to perpetuate their disability. They show subtle resistance to even the threat of effective treatment. They "cultivate their pain, pay great attention to it, support it, amplify it, and protect it." Of course true pathologic states, like causalgia, causalgia-like syndromes, and painful neuroma must not be overlooked and when present must be effectively treated. But these patients show no major nerve injury, are relieved by local anesthetic block of appropriate nerve and nerve roots but gain no relief from sympathetic nerve block. Shaw offers some important pointers in therapy also. We must be careful not to make the patient believe that our diagnosis is pathologic malingering. He will take immediate flight. Of absolute primacy in treatment is the removal of the patient's motivation to remain disabled. We must try to ellicit, usually from others, what the patient is trying to escape from or gain. Is it monetary reward, a pending law suit, inadequacy or insecurity he would face if not disabled?

In the usual case in which the primary value of the disability is financial, obviously the solution must come from the courts, the seat of ultimate authority. It is rare that a strong-willed confident doctor succeeds in setting a man back to work without it. Unless there is authoritative removal of the promise of reward for disability, treatment is hopeless and is usually both angering and frustrating to the attending physician. Psychotherapy is unrewarding and active physcotherapy makes things worse. And of course, unnecessary operations and procedures compond the disability.

When the gain is removed from the disability, there may be a miraculous, spontaneous rehabilitation, well documented by Miller.[3] The secondary physical changes from prolonged disease may persist for a while, so may the secondary psychologic atrophy of normal motivation or fear of loss of face also persist for a while. Soon, however, contractures and muscle atrophy will respond to physiotherapy and resumption of function. At this time the patient needs an explanation for the painful physical results of desire and the mechanism of their reversal. Enthusiastic discussion of the patient's plan for the future is now in order as well as strong emotional support from a physician to whom the patient has an attachment.

Inasmuch as the only real solution rests upon elimination of the basic problem of gain by the patient from his disability, the physician is duty bound to state that the patient disabled by pain is a motivational malingerer. The physician must pursue the truth in court and not make the truth subserviant to the patient's wishes. Failure to reveal the true nature of the patient's problem unhappily tends to perpetuate a fraud on society, keep the patient pathological and tends to raise havoc with the legal and public image of the physician.

Shaw has seen the situation complicated, as we all have, by violent disagreement among experts, the psychiatrist, whether such pathologic malingering is conscious or unconscious; the medical professors who can compound the problem by diagnosing "Sudeck's atrophy," "reflex sympathetic dystrophy," or "traumatic arteriospasm" and perform sympathectomy or mutilating neurosurgical procedures in an attempt to relieve pain. He has even seen, fortunately rarely, when a well intentioned physician established narcotic addiction to relieve his patient of pain.

It is probable that a clearly defined diagnosis of pathologic malingering as a clinical entity, with a specific cause would go a long way towards mastering this problem and become a key to its solution.

L.H.N.

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Rapport:

2. Trust As A Factor In Rapport

The real question is how do we bring rapport about? First of all we must try to sense whether the patient is secure with us. We must see quickly whether he can trust us with his real problem. In such a situation it is very tempting to use logic, to put the situation to the patient logically. It is useless to say "I am your doctor you can trust me." This is factual and true. We have seen, however, that rapport is an emotional relationship and that it is established not by logical processes but rather by emotional mechanisms. There is danger that the logical statement that the patient can trust the physician may in fact have the very opposite effect. Generally, in most life situations only people who are not quite worthy of our trust make open statements about being trustworthy. In fact somehow bringing a logical critical element into a relationship may even hinder the easy feeling between two human beings that must be the basis of trust. Our academic appointments and standing in the profession may give us prestige with the patient, but they do not make it easier for him to trust us, since rapport is a personal man-to-man relationship, not patient to physician relationship.

Before we can trust anyone we must get to know something about him as a person. Just knowing that the man we are talking to is a doctor is not enough to enable us to give him our trust. The fact is, and doctors must realize this, that as we proceed to find out the patient's problems, he also sets out to find out what sort of a person we are. He scrutinizes us, and if he is an anxious patient, it may be very obvious and at times penetrating. Unless we are aware of the need for the patient to examine us in this way, it may make us hostile. The fact is we must graciously accept the patient's right to examine us, yea even the necessity for it. If we do not do so he cannot trust us, if we make it easy for him, then he can.

It is not wasted if we devote a few moments of inconsequential conversation when we first meet. It gives the patient the opportunity to know us a little and he can begin developing trust in us. At the beginning we must be careful not to ask any question that requires thought or will engender worry. We must give him a chance to assess us at his leisure. Usually if we do not rush the patient, his scrutiny will not take much more than a few moments.

The easiest way of course to lead someone to trust us is to show him that we in fact trust him. But we do not do this by telling the patient we trust him. This would sound incongruous and inappropriate to him. It might alert him and render him suspicious of us. How then can this be done? It can be done—somehow we can communicate the idea to him through certain symbols of trust. One way is to let him know how we feel by allowing normal expressions of emotion to cross our face or by an assuring gesture. We trust him by some little bit of personal information. We trust him by making the next appointment with him not with a relative. We trust him by making him, not a relative, responsible for the administration of his own drugs. These are many similar small things but they symbolize a greater trust. The patient himself may not be consciously aware of it, but somehow these evidences of trust in him leads him to trust us.

It is hard to trust anyone who presents a facade. We trust those who in one way or another disclose something of themselves to us, those who hold back little, those who do not hide behind an artificial front. A neurotic notoriously operates behind a false front. It is his resistance to disclose the significant information, which is the reason why the patient in psychoanalysis takes so long to disclose his emotionally suppressed wishes. The neurotic patient feels that he does not know his analyst and it takes him a long time before he can trust him with the really important information. To a lesser extent this is true in general even in the absence of neurosis. As physicians we must aim to avoid this though there are often difficulties.

It is not easy to let the patient see us as we are, particularly if we ourselves are operating behind a facade. This is more true of the insecure younger physicians who may assume a would be sophisticated manner to offset his immaturity in early practice. This of course fools no one, especially the patient. As experience grows, however, our knowledge of human beings increases, our security in our relationships with patients becomes solidified. Every patient knows the doctor is not omniscient, and suspects the doctor who acts so. We do not reduce our image by concealing our shortcomings. The patient will no longer look to us as he has in the past. He begins to look at us in a different way, neither as a glorified figure of the imagination, nor as a person trying to hide his shortcomings, but

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as a real person whom he can trust. When this point is reached the patient talks openly to us and freely and there is no holding back.

And so we as physicians must guard against an unconscious or conscious attempt to present a facade. As far as we can, we just let the patient see us as we really are, a person with assets, a person with shortcomings, who recognizes them and is striving to overcome them. What an excellent example this could set for our patients who also should strive to overcome deficiencies. When the patient realizes that we are secure in ourselves, that we do not hide our shortcomings, if we let him know something about an occasional failure, he quickly comes to give us his complete trust. Of course, it must be sincere, there must be no pretense about this. Meares[1] even goes out of his way, when a patient wavers in his trust, by deliberately disclosing himself in this way. Invariably he has found the patient returns the doctor's trust with his own.

L.H.N.

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Weight Loss Without Hunger

Prolonged use of low calorie diets is always associated with hunger. The two components of hunger, generalized weakness and a perception in the epigastric region of intermittent sensations of tension or pressure, may be the real reason why low calorie diets by themselves are so often unsuccessful in a prolonged weight reduction regimen.[1] The patients seem to develop a preoccupation with thoughts of food. They tend towards irritability and depression. With this goes some loss of initiative. It is not surprising therefore why it is that low calorie diets do not solve the problem of eliminating obesity. To eliminate the psychologic manifestations of low calorie diets, physicians have resorted to anorexic and antispasmodic drugs like amphetamine. Such drugs do assist some people in achieving better spirits, a more energetic outlook and a larger sense of well-being. But when such drugs are discontinued, hunger returns and the relapse rate becomes very high. Besides this, many patients soon find ordinary dosages inadequate to curb their appetites and again a relapse occurs and the patient returns to his old eating habits.

Throughout all history fasting, a logical answer to overeating, has been considered a useful plan and has been adopted in religious ritual, fads, and some medical practice. In many areas physicians have found that fasts lasting over 48 to 96 hours produced virtually no hunger and were usually well tolerated and seemed safe. Various methods of weight reducing employing starvation have been proposed; such as repeated periods of 10 days to 2 weeks fasts; some with starvation up to a month or longer have been described. All the reports emphasize that prolonged fasts are easily tolerated; little discomfort is experienced, and no serious side effects were observed. The limits of the starvation period in obese subjects which is compatible with good health has not been established. What we also need to know are the factors that limit the duration of starvation in obesity; and the clinical and metabolic changes which might occur during the starvation.

Drenick et al[2] have studied 11 patients who were hospitalized in a metabolic balance ward. The weights ranged initially from 240 to 450. Each was allowed water ad lib and given a multivitamin pill to avoid the real danger of avitaminosis. Many blood constituents were studied and urine examined. The surprising outcome of this study was that the hunger sensation was present only the first 2-4 days after the last meal, after which it disappeared completely. Even in the first several days hunger was surprisingly mild. At the beginning patients took water freely but then after awhile thirst abated and water consumption decreased drastically and with it the urinary volume. In those fasting for two months water became very unappetizing. Elimination of fecal material ceased after 3-4 days. Then small amounts of mucoid material were evacuated at 2-3 week intervals. On resumption of eating, bowel activity proceeded normally.

Physical endurance decreased slowly but severe weakness was uncommon. The older patients tired more easily, but the younger ones remained fairly vigorous and some could do physical work. The sleep patterns were not altered. Blood pressure declined to normal while the pulse rate and respiratory rates declined little. The most obvious result of starvation was weight loss. One female who starved 117 days lost 116 pounds. However, only one patient could get his normal weight back in one single continuous period of fasting. The initial weight loss was prodigious. One patient lost 9 pounds the first day but most lost 2-3 pounds daily for the first 10 days then the weight loss per day gradually fell until it was 0.7 pounds daily after the first two months.

As might be expected, once carbohydrate stores are used up, then animo acids are used for gluconeogenesis and this means greater excretion of nitrogen, mild ketosis from shifting metabolism towards oxidation of fat, and accumulation of uric acid in the blood from destruction of large numbers of cells. Because of the hyperuricemia two patients developed gout. Because of absence of positive protein balance, almost half of the patients developed an anemia during the second month, refractory to iron, B12, but promptly responding to refeeding.

From Drenick's work it is clear that prolonged starvation was tolerated with ease as compared with hunger and suffering described by individuals who over a prolonged period consume a calorically inadequate diet. In fact as the fast proceeded it seemed to become easier tolerated. The rapidity of weight loss not only produced no side effects but actually relieved patients who suffered from respiratory or cardiovascular embarrassment. What was equally striking was that those who attained a normal body weight were enthusiastic and delighted to resume living as normal weight human beings. Even more striking was the radical change in the eating habits. They continued to eat substantially smaller amounts of food than prior to starvation, and seemed to have little difficulty in maintaining their weight.

The only two manifest problems encountered were hyperuricemia which developed in all patients and postural hypotension which developed only in some. Orthostatic hypotension became noticeable after the 3rd or 4th week and was associated with extreme weakness, faintness and syncope upon rising out of bed. The blood pressure in one patient dropped from 180/120 to 70/40 and nothing really helped. It is obvious if a patient has coronary insufficiency or cerebral ischemic disease, he would do well not to fast long enough to develop postural hypotension.

Because of the side effects of hyperuricemia, postural hypotension, anemia, prolonged fast cannot be viewed as a panacea for all obese individuals. The desire of the starving unhungry patient to pursue the treatment to effect a drastic weight loss quickly, can lead to certain dangerous consequences. Drenick's work will make physicians and patients aware of some of the hazards which may result from prolonged periods of food privation and should perhaps encourage shorter fast periods and repeated ones, until the normal weight is finally reached.

At the present time it is not possible to compare the results obtained in prolonged starvation with those in prolonged use of low calorie diets. It is not difficult to improve uric acid clearance and it ought to be possible to elucidate the mechanism of postural hypotension. Even then, what will be the long term effects of reduced metabolic and physical activity on the starving patient? And what will we see in these starving patients a year or more after their fast? One thing we do know, the end results of total calorie restriction has not been good. And so despite the hazards of starvation it seems that in certain excessively obese patients, the gratifying weight loss without hunger, may bring about the desired results and help establish a normal eating pattern where other dietary restrictions have failed.

L.H.N.

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Suppression Of Glandular Activity: 3. Periodic Hyperadrenocorticism

An almost universal phenomenon in biology is the existence of cycles,[1] from photoperiodism in plants to bird migration, to menstruation and many other less obvious instances. In animals most obvious cycles originate in the central nervous system. Cyclic production and release of hormones is characteristic of endocrine regulation of physiologic central mechanisms, the most obvious being menstruation in which the pituitary-gonadal axis operates. Now comes a case reported by Wolff, et al.[2] who describe a disease state involving a suspected hypothalmic lesion together with periodic and augmented release of ACTH, and adrenal-cortical hormones. A fourteen year old boy showed cyclic manifestation of nausea, vomiting, fever, emotional disturbances and marked weight change. During the attack the patient developed facial plethora, hypertension, abnormal glucose tolerance, elevated plasma ACTH and adrenal hyperfunction. The patient's usual weight before an attack was 75 kg. However, during his attack he lost five to ten kg. which could be accounted for by loss of water due to vomiting, urination or sweating.

The cyclic nature of the disturbance really started at the age of six when he began to have recurrent episodes of nausea, vomiting, fever, mental depression and marked weight loss lasting three to five days and recurring irregularly every six to twelve weeks. At the age of ten the episodes became periodic and recurred every three weeks. The periodicity was so striking that the family made no social or other plans for the anticipated time of the attacks.

The young patient was observed at the National Institute of Health on several admissions, the first one for about twenty-one weeks during which he had seven episodes which usually began in the morning. Each attack lasted four to five days every three weeks. It is astonishing how many laboratory tests were performed on this young patient. G.I. series, EEG., ECG., pneumoencephalograms, in-

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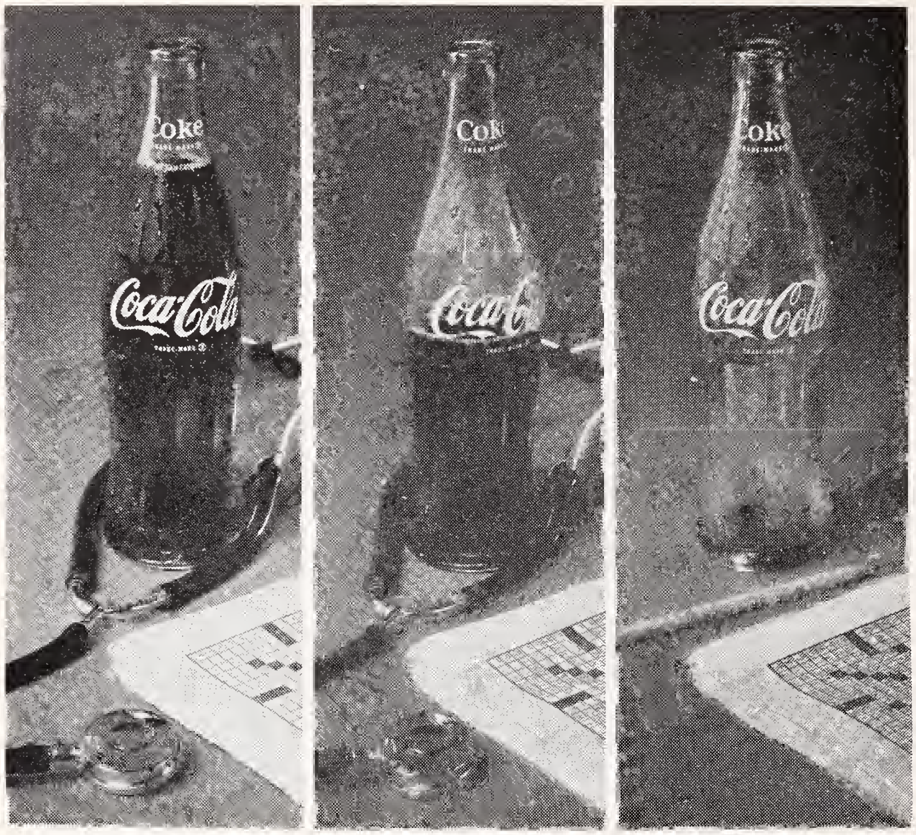

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numerable blood tests for hormones, electrolytes, cholesterol, serum lipids, triglycerides, glucose phospholipids, and innumerable urine tests for hormones and their degradation products, electrolytes and other excretion products too numerous to mention. Tests were done for pheochromocytoma, for neurological deficits, for infections, and extensive metabolic studies were also and repeatedly carried out in a well organized attack on the hidden nature of the periodic disease. In the end it became clear that some aberration of the hypothalmic-pituitary adrenal axis was involved and there occurred periodic release of ACTH which in turn caused a flooding of the system with cortisol and DOCA that led to the observed clinical signs and symptoms.

We are beginning to recognize a wide variety of clinical disorders which have been classified as periodic disease as well as the numerous periodic physiologic episodes that occur normally.[3] During the past few years such diseases as Mediterranean fever[4] and etiocholanolone fever[5] have been identified. When an unusual recurrent fever occurs extensive evaluation can lead to placement of some of these patients into well recognized disease categories. Even then the patient reported by Wolff, et al. would appear to represent a unique and hitherto unreported complex of symptoms and signs.

The anterior portion of the pituitary, and thus the release of ACTH, has been identified as at least partially under the control of the hypothalamus through neuro-humoral mechanisms. However, in the vast majority of the hypothalamic disorders and abnormalities of ACTH release, the resulting disorder is one of hyposecretion of corticotrophin not one of increase, as was present in this case. Whatever triggered the cycle it was not caused by environmental influences but by some internal mechanism.

The authors proceed deductively to search for the trigger without much success although the explanation of the individual symptoms is readily derivable from the disturbed hormonal secretion. The fever could be due to elevated plasma unconjugated etiocholanolone but involvement of the thermoregulatory mechanism in the hypothalamus could not be ruled out. The massive vomiting could be due to hypersecretion of catecholamines which can cause gastric dilatation and result in vomiting. The hypertension seemed to the authors as caused by hypercorticism which probably is the basis also for marked changes found in glucose metabolism.

The treatment of the patient followed logically from the recognition of the basic fault. If excessive ACTH secretion is at the bottom of the disease, then suppression of the anterior pituitary cells secreting ACTH should relieve the syndrome. In fact, the pituitary was suppressed with large doses of dexamethosone and the patient was free for many months, but every time the dose was tapered, the syndrome "broke through," and when this happened the blood again showed a rise in ACTH.

We thus have a case in which extensive laboratory testing and beautiful reasoning based upon newer knowledge of endocrinology, has illuminated for us many physiologic mechanisms involving the interaction between the hypothalamus, pituitary and adrenal gland. We would do well to familiarize ourselves with the dynamics in this case of periodic hypothalmic discharge.

L.H.N.

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Iron Balance

The characteristic and easily recognized ferritin molecule seen by electron microscopy has served as an invaluable fingerprint in tracing the course of iron through the body.[1] Utilizing this as one method of study Dr. William Crosby and his group at Walter Reed Army Medical Center have recently clarified the subject of iron absorption and excretion in an important series of articles published in Blood.[2,3,4,5] The material is collated in an editorial review[6] from which the following schema is summarized.

Day to day control of iron balance is largely carried out by the ferritin apparatus of the absorptive epithelial cells of the upper small intestine. Information on the body iron needs is brought to these cells, possibly by the relative concentration of plasma iron or iron binding capacity. If the body iron stores are low, new formed epithelial absorptive cells possess no ferritin apparatus; iron is therefore readily absorbed and carried through the cells to the blood and thence to the liver, bone-marrow and other tissues. When the iron stores are full, new epithelial absorbtive cells do have a ferritin apparatus by which a cell protein, apoferritin, reacts actively with ferric iron to form ferritin from which iron can be released only with difficulty. If iron succeeds in entering the intestinal villi despite the ferritin barrier, much of it is absorbed by macrophages and brought back to the epithelial surface. Both macrophages and ferritin-filled epithelial cells ultimately reach the intestinal lumen and are shed via the bowel. This shedding mechanism can get rid of about 5 mg. of iron daily. In addition to this excretory effect the iron-filled cells resist iron absorbtion.

When this mechanism fails and iron gradually accumulates in the tissues the secondary harmful effects are then manifest in the form of hemosiderosis and hemochromatosis.

R.N.B.

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New Oral Contraceptives

Since The Medical Letter last appraised oral contraceptives (5:34, 1963), several new products, all combinations of estrogens and progestagens, have been marketed. The chief innovation has been the reduction of the doses of the progestagen component. Thus, Enovid, the first of the oral contraceptives, contained 10 mg. of norethynodrel; it is also offered in a 5-mg. tablet and as Enovid-E, with 2.5 mg. of norethynodrel.

The combination of estrogen and progestagen not only inhibits ovulation, but also brings about changes in the endometrium which assures adequate and predictable withdrawal bleeding. A new method of administration, 15 days of an estrogen alone followed by five days of a progestagen, is being tried, but its reliability is not yet known.

Thromboembolism—There is no dispute about the effectiveness of the combination contraceptive drugs now on the market; the new preparations, like the older ones, if used as prescribed (one tablet daily for 20 days beginning the fifth day of the menstrual cycle), appear to be completely successful in inhibiting ovulation. There is, however, dispute about their side effects. The most immediate concern relates to the risk of thrombophlebitis and pulmonary embolism. In a Final Report on Enovid submitted to the Food and Drug Administration by a special committee, September 12, 1963, it is stated that "There is a need for comprehensive and critical studies regarding the possible effects of Enovid on the coagulation balance and related production of thromboembolic conditions. Pending the development of such conclusive data and on the basis of present experience this latter relationship [between thromboembolism and the use of oral contraceptive pills] should be regarded as neither established nor excluded."

Long-term side effects — Whether serious long-term effects—over a lifetime—can occur will not be known for many years. Enovid has been used for more than eight years in Puerto Rico (at first with 10 mg. of norethynodrel, later with 5 mg., now with 2.5 mg.), and studies there have so far shown no evidence of endocrine damage, changes in the hemogram, or carcinogenesis. A few instances of aggravation or precipitation of diabetes mellitus have recently been reported. There is no evidence that the drug has a lasting effect on fertility; discontinuance after long-term use has resulted in rapid restoration of fertility.

All manufacturers' package inserts caution about the use of the drugs in liver disease. Masculinization of the female fetus might possibly occur if the pills are taken during the early weeks of an unsuspected pregnancy. Contraindications to the use of oral contraceptives are a history of thrombophlebitis or embolism, and malignancy of the breast or uterus. Oral contraceptives, like pregnancy, may stimulate the growth of existing fibroids. The pills should not be taken by girls who have not reached full growth, since estrogens are known to accelerate closure of bone epiphyses.

Other side effects—The most common side effect, nausea, frequently disappears in a month or two. While it lasts, taking the daily pill before bedtime or with the evening meal usually helps. Other side effects are breast fullness and breakthrough bleeding. Mild fluid retention is common. Mental depression has frequently been observed, but whether it is due to the hormones or to emotional factors is unknown. Chloasma is a rather frequent side effect. The reduction of progrestagen dosage appears to have lessened the frequency of nausea and possibly other side effects.

Oral contraception may be begun at any time after labor unless the patient is nursing; it is contraindicated in nursing mothers, since the estrogen excreted in the milk may cause enlargement of the baby's breasts. A patient in menopausal years may be advised to discontinue oral contraception and to use other means of birth control for six months. If she menstruates, oral contraception is recommended for 12 more months followed by another period of discontinuance.

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Problems In The Treatment Of Cancer

Alton Ochsner, M.D.

■ Problems in the treatment of cancer depend on the type, location, relative degree of malignancy, and duration of the lesion. The desideratum in the treatment of malignant disease is complete eradication of the growth, which is possible only if the lesion has not metastasized.

Although some believe that the treatment of cancer is futile because the ultimate result depends upon complete predeterminism of the tumor, I am convinced that such is not the case. Admittedly, there are exceptional cases in which this hopeless outlook holds, such as the extremely small lesion which is detected early and treated adequately but in which widespread dissemination has already occurred. Conversely, we see individuals with large tumors which have existed for longer periods of time but remain localized and are cured by simple excision. These two instances, of course, represent the extremes, and in such cases the urgency of diagnosis is unimportant. Such is not the case, however, in most cases, which fall in the median segment. In general, the earlier the diagnosis is made and therapy instituted, the better the prognosis because the chances of eradicating a neoplasm are greater when it is in the early stages of development.

The American Cancer Society has done a real service to the people of the United States by emphasizing the need for periodic examinations in order to detect not only malignant lesions but also premalignant disease. In fact, it is even more important to detect and treat premalignant lesions than malignant disease because in this way the latter can be prevented. Criticism of the American Cancer Society for fostering a "scare program" is unjustified. It is true that some people become panicky if they think they may have cancer, but a healthy fear is necessary to make people seek treatment for a condition which is not bothering them very much. If cancer caused pain in its early stages, we would have little difficulty in making the diagnosis early. There may be a few patients who have acquired cancerphobia as a result of the educational program of the American Cancer Society, but these persons originally were psychically unstable and if they did not get cancerphobia, they would acquire some other phobia, such as concern about their spouse or their heart. More than 90 per cent of persons, however, have been helped by this fear of cancer because it has made them consult their physicians about insignificant disturbances or at regular intervals so that early malignant disease and even precancerous lesions have been detected.

Since the surgical treatment of cancer, which consists of removal of all or a major portion of the malignant viscus together with the regional lymph nodes, has been placed on a firm scientific basis, much has been accomplished. However, it has long been recognized that at times cancer may extend beyond the regional lymph nodes not only by means of the lymphatic system but also by invasion of the blood vessels. Whenever malignant cells extend beyond the areas which can be surgically excised *en bloc*, there is a possibility of distant metastases. However, since the widespread use of cytologic methods of examination of the blood, it has become evident that neoplastic cells often enter the vascular system and circulate in the blood stream without producing distant metastases although the potentiality is there.

About three years ago Dr. Hurst Hatch, who is in charge of our Pulmonary Function Laboratory, reasoned that if the blood in a vein draining a viscus contains a higher percentage of neoplastic cells than blood in the systemic circulation, in carcinoma of the lung examination of peripheral arterial blood would be comparable to examination of the blood in the pulmonary veins, since this blood goes directly to the left side of the heart and then out into the systemic circulation. He and his coworkers have now examined the peripheral blood of more than 100 patients, studied in the Pulmonary Function Laboratory. Of those with proved bronchogenic carcinoma, 40 per cent had neoplastic cells in the peripheral arterial blood. If the lesion was in the hilar region, the incidence was 30 per cent, and if it was in the peripheral area, it was 70 per cent. We do not yet understand the significance of this high incidence of involvement in the peripheral arterial blood but we are not altering

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our indications for treatment and hope that in time we will be able to evaluate this observation.

Some malignant tumors offer real problems because of their location and because of the positive symptoms which they produce. For example, carcinoma of the pancreas is one of the most difficult tumors to treat primarily because it is almost impossible to make a diagnosis in the early stages of the disease. Unless the lesion happens to be in the head of the pancreas and early constricts that portion of the common duct traversing the head resulting in jaundice, the patient with carcinoma of the pancreas usually has no symptoms until the disease has extended beyond the pancreas to involve the parietes, at which time pain is produced and there is much less likelihood of successful extirpation.

Carcinoma of the esophagus may be present for a long time before a diagnosis is made primarily because of the tremendous capacity of this structure for distention so that the lesion can be relatively large without producing many manifestations. Although esophageal lesions are readily amenable to radiologic and endoscopic examination, unless the physician is alerted to the possibility of an esophageal lesion, these diagnostic procedures may not be used early enough to make a diagnosis at the optimum time for cure. Treatment of carcinoma of the esophagus by irradiation or surgical extirpation has been unsatisfactory because of remote metastases via the lymphatics. Irradiation may completely destroy the esophageal lesion and produce satisfactory palliation but will not result in cure because of extensive involvement of the intra-abdominal lymph nodes.

The results of treatment of carcinoma of the stomach have not been good largely, I believe, because of delay in instituting appropriate therapy. If we wait until carcinoma of the stomach can be diagnosed, the disease is usually too advanced for curative treatment. Although gastric carcinoma is not a new lesion in contradistinction to bronchogenic carcinoma, the results of treatment today are not much better than they were twenty-five years ago. The five year survival rate is about 10 to 12 per cent of all the cases in which the diagnosis is made. Japan is probably the only country where better results are being obtained. There, the incidence of gastric carcinoma is higher than in any other place in the world and the entire population is cognizant of this so that patients with any digestive disturbance consult a physician early. Japanese physicians also have excellent intragastric cameras which photograph the stomach and make possible relatively early diagnosis of gastric neoplasms. For this reason, their overall five year survival rate is considerably higher than in the United States. I have long believed that the results of treatment of gastric cancer will not be improved if we wait until we can diagnose it by gastric analysis, roentgenography, and gastroscopy, because when the diagnosis is established by these methods, the lesion is far advanced. I believe that lesions which clinically are not gastric cancer, such as gastric ulcer, gastric polyps and certain cases of atrophic gastritis, especially those associated with pernicious anemia, should be treated surgically. The only optimistic note about gastric cancer is that the incidence is definitely decreasing, being about half as common today as it was fifteen years ago. It and cancer of the cervix are the only two cancers whose incidences are decreasing in the United States. I attribute this to the fact that precancerous cervical and gastric lesions are being detected and corrected before cancer develops. The precancerous lesion in the stomach is gastric ulcer, I believe, and since an increasing number of physicians think, as I do, that all gastric ulcers should be removed, gastric cancers are being prevented.

The cancer whose incidence is increasing more than any other in the United States is bronchogenic cancer. This lesion was extremely rare forty years ago. Originally it affected males and females with equal frequency, but has become much more frequent in males than in females and now exceeds both cancer of the breast and the female genital tract. Bronchogenic cancer is preventable, I believe, because with the exception of adenocarcinoma, which is an extremely rare type of broncogenic carcinoma, this disease is caused by cigarette smoking. It is particularly unfortunate that the incidence of bronchogenic carcinoma is increasing because rarely can the diagnosis be made at a time when therapy can be successful. The five year survival rate in an extremely large series of cases at the Ochsner Clinic is about six per cent, which is the same as that reported by others with considerable experience. I doubt if this is going to be improved. Therefore, it behooves all of us to try to prevent this tragic and rapidly fatal type of cancer by emphasizing the danger of cigarette smoking.

Although previously I believed that the treatment of cancer of the lung was pneumonectomy because not only the viscus but also the regional lymph nodes could be excised much more readily, I subsequently have become convinced that limited resections are just as efficacious. I now perform lobectomies and even segmental resections in certain cases of bronchogenic carcinoma. Although the concept of pneumonectomy with wide resection of the mediastinal nodes is still good because it represents a better cancer operation, the results do not justify it because of early invasion of blood vessels and wide dissemination, which offsets the advantages derived from the wider resection of the pulmonary lesion.

The incidence of cancer of the colon is also increasing although much less than is cancer of the lung. The reason for this is not obvious. However, cancer of the colon usually offers a fairly good prognosis because of the relative ease with which a diagnosis can be made at a time when the lesion is resectable. It is becoming increasingly more evident that wider resection of the colon than previously used is desirable. Whereas right colectomy has long been the treatment for right-sided lesions of the colon with good results, until recently segmental resection was employed for left-sided lesions with much less favorable results. Recently, however, resection of the entire left colon for lesions of the descending colon and sigmoid has been advocated.

Another malignant lesion which presents problems because of the almost universal misconception concerning its treatment is melanoma. Unfortunately, some physicians believe that treatment of a mole which has changed character and which probably is a melanoma can be relatively simple and is of little significance. Conversely, others believe that a melanoma is so highly malignant that treatment is futile. Both of these concepts are fallacious. Although malignant melanoma is an extremely malignant disease, the prognosis is not bad if it is treated as a highly invasive malignant tumor. Also, one must be aware of the unpredictability of this lesion, since it may appear to be controlled for a long time and suddenly flare up for no apparent reason. Treatment of any mole which might be malignant consists of wide excision and careful histologic examination to determine whether it is latent. If it proves to be malignant, much wider excision should be done down to and including the fascia. The extent of the incision should be large enough to require grafting. There should be concomitant regional lymph node dissection. If the lesion is in the vicinity of the lymph node, *en bloc* excision of the fascia between the original tumor and the regional lymph nodes should be done. If, however, the originating lesion is some distance from the regional lymph nodes, such as on the foot, wide excision of the original lesion and concomitant lymph node dissection should be done. I do not like to consider this as prophylactic lymph node dissection, because even though lymph nodes are not palpable, it is being done as a curative procedure and to remove involved nodes which are not palpable. Our experience definitely shows that if one waits until the regional lymph nodes are obviously involved, the results are not as good as in those patients in whom concomitant lymph node dissection is done at the time the original tumor is removed. With the availability of regional perfusion, we no longer amputate the lower extremity, but if satellite lesions do develop, we perfuse the extremity with equally good results as after amputation and the extremity has been saved.

Treatment of metastatic malignant lesions of the lung also poses a problem. Our experience indicates that in certain of these patients pulmonary resection is justifiable provided certain criteria are fulfilled. These are that the patient has no evidence of metastases elsewhere, his physical condition is otherwise good, and he and his family understand that he probably has other metastatic lesions which are not detectable. Resection should be as limited as possible without sacrifice of any unnecessary pulmonary tissue. This can be accomplished by segmental resection, wedge resection, or lobectomy. Occasionally, however, because of the location of the lesion pneumonectomy becomes necessary. In 28 operations on 25 patients with metastases to the lung the survival rate was 27 per cent at five years and 20 per cent at ten years. The shortest survival rate was three months, the longest 167 months, and the mean 12 months.

In follow-up study of our patients with cancer we have attempted to follow all of them. We believe that in the treatment of malignant disease survival statistics should include all cases rather than only those who survive the surgical procedure. Unfortunately, in the United States it has become common practice for surgeons to base follow-up results in the surgical treatment of malignant disease only on patients who survive the operation. I have long maintained that the operation is just as much a part of the disease as is the disease itself, because the more extensive the disease, the more dangerous the operation. Were it not for the disease, the operation could be performed with relatively little risk.

Several years ago, I heard a prominent surgeon report good five year results in the treatment of bronchogenic carcinoma. He stated that he did not include his operative deaths because the patients who did not survive the operation could not survive five years. This is certainly true because according to this same reasoning patients could not survive five years if they had not survived four years, so why not use survival at four years as a base line?

The survival rates of the various kinds of carcinomas vary widely. In bronchogenic, gastric, colonic, and uterine carcinoma there is a rapid drop of the survival rate down to about the third year, after which a plateau is reached. This is not true of carcinoma of the breast and certainly not of melanoma. It is well known that the patient with carcinoma of the breast can be apparently well for fifteen or twenty years and then have a recurrence or evidence of metastasis. This is also true of melanoma, for survival of five years after treatment of melanoma with no evidence of metastasis does not mean that the patient is cured. I first appreciated this about thirty years ago when I saw a patient with a lesion of the lung which I thought was malignant who also had had an eye enucleated twenty-five years previously for a presumed malignant tumor. Unfortunately, I was unable to get the histologic diagnosis of the tumor of the eye. Because twenty-five years had elapsed since enucleation of the eye and appearance of the pulmonary lesion, I believed that there could be no relationship between the two. At operation a melanoma was found and was satisfactorily resected but within eight months the patient was dead from extensive melanosis.

Another peculiarity of malignant tumors is that the systemic manifestations of some vary considerably. This is particularly true of melanoma and carcinoid tumors. A patient with a melanoma may have extensive involvement of the skin and viscera and yet be relatively asymptomatic all his life. This is also true of carcinoid, particularly if the liver is extensively involved; the only exception is the occasional patient with flushing. The patient with the carcinoid syndrome may remain in good health with relatively few symptoms for twenty to twenty-five years, even though the liver may be almost completely replaced by tumor.

In conclusion, it is hoped that when the factors responsible for the change of the normal growing cells into malignant cells are discovered, the problems which have been discussed will no longer exist.

The Experimental Method

Reasoning will always be correct when applied to accurate notions and precise facts; but it can lead only to error when the notions or facts on which it rests were originally tainted with error or inaccuracy. That is why experimentation, or the art of securing rigorous and well-defined experiments, is the practical basis and, in a way, the executive branch of the experimental method as applied to medicine. If we mean to build up the biological sciences, and to study fruitfully the complex phenomena which occur in living beings, whether in the physiological or the pathological state, we must first of all lay down principles of experimentation, and then apply them to physiology, pathology and therapeutics. Experimentation is undeniably harder in medicine than in any other science; but for that very reason, it was never so necessary, and indeed so indispensable. The more complex the science, the more essential is it, in fact, to establish a good experimental standard, so as to secure comparable facts, free from sources of error. Nothing, I believe, is today so important to the progress of medicine.—Claude Bernard, M.D. *An Introduction to the Study of Experimental Medicine.* New York, The MacMillan Company, 1927, p. 2.

The Management Of Allergic Patients In Office Practice

Douglas E. Johnstone, M.D.

The practical management of allergic patients is virtually a daily problem for busy physicians. The incidence of major allergic syndromes in this country is said[1,2,3,4] to be between ten and twenty per cent. In a survey of several thousand children in the northeastern section of the United States, Appel Szanton and Rapaport[5] found that twenty per cent suffered from a major allergy such as hay fever, asthma, atopic eczema or perennial allergic rhinitis.

The success in treating these common problems may be influenced by the kind of treatment the patient has received, by the amount of exposure to potent allergens he has had, and by his constitutional makeup. Another important factor may be the degree of cooperation between the patient or his parents and his physician. This, in turn, may be influenced by available housing, as well as financial, ethnic, intelligence, medical and psychological factors. Finally, the natural history of the specific syndrome a patient has may be such that it will disappear spontaneously.

Some of these common allergic problems are simple and are easily managed by the general physician, pediatrician, internist. Some will be more complicated than the physician feels he has the time or training to manage properly. Unfortunately, in the second situation there may be no specially trained person nearby to whom a physician can refer the patient for an allergy consultation. He must do the best he can. This requires first a knowledge on his part of what is the optimal treatment for a patient's individual problem. He must be prepared to take the time necessary to do a careful job. The first step is to take a careful history. This may take up to an hour, either at one sitting or in several shorter visits until an adequate history is obtained. Finally, he must be honest with himself. If he finds he needs help, he must heed the needs of the patient and seek consultation with someone who is more experienced than he in handling allergic patients. Although a few allergic problems respond poorly to expert care, increased knowledge and new techniques permit gratifying results in the majority of allergic problems. Part of the problem of the physician without formal allergy training is to familiarize himself with which clinical problems lend themselves to solution with modern allergic management.

The following outline will be used for the discussion of the management of the commonest major allergic syndromes:

1. *Natural history of the disease.*
2. *Prophylactic measures.*
3. *Symptomatic management of symptoms.*
4. *Criteria for skin testing.*
5. *Specific hyposensitization therapy.*

Atopic Eczema

1. *Natural history.* Atopic eczema is an eruption of the skin characterized by erythematous, papulovesicular moist lesions which tend to develop crusts. Common features include (1) predilection for certain locations such as the antecubital and popliteal spaces and occasionally the face and other areas, (2) intense itching, (3) tendency to secondary infection, (4) high incidence of atopic disease in the family history, and (5) a tendency to develop respiratory allergies.[6] Eczema often begins in the first three months of life. In the majority there is complete clearing of the skin, with or without specific treatment before the fourth birthday. In a few children[7] eruption persists until adolescence. Rarely it may persist beyond adolescence.

2. *Prophylactic measures.* Grulee and Sanford[8] reported that breast fed infants had only one-seventh the chance of getting atopic eczema as the bottle-fed baby. However, infants in that era did not get early solid feedings of wheat, egg, chicken and beef. Glaser[9] reported that one might prevent eczema or at least lessen the tendency to develop subsequent respiratory allergy following eczema if potentially allergic newborns were placed on a diet free of the commonest offending foods such as egg, wheat, milk, beef and chicken. He found that children placed on such a diet from the time of birth through the first nine months of life de-

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veloped only a fourth as many major allergies as their siblings. Of those placed on this diet who did develop atopic eczema the incidence of subsequent major respiratory allergy was only one-fifth as great as in eczematous siblings.

Because of the tendency of eczematous children to develop respiratory allergy every effort should be made to minimize exposure to air-borne inhalant allergens from the time of birth. Finally, these children must not receive or be near children who recently received a small pox vaccination.

3. *Symptomatic management.* In general one should try to avoid suspected allergens, to do nothing to injure the skin or impede healing and to do what one can to treat any secondary infection and promote healing of an itching inflammatory skin lesion.

In the first year of life foods are often the important cause of eczema. Thereafter inhalants become more important causes. The first step in dietary manipulation should be a trial of an elimination diet. Ideally, all potentially allergenic foods should be eliminated simultaneously, rather than eliminating foods one at a time. If parents and patient will cooperate, one may begin by giving soybean milk or lamb base meat milk formula along with drinking water as the only food for three days. During the second three-day period lamb or pork is added to the diet. In the third three-day period sweet potato is added. If foods are the major etiologic factor in the patient's eczema, one should note at least a lessening of his itching. Other foods and vitamins may then be added every two to three days, keeping a food diary of the sequence of addition of foods. In some children, foods are only a part[10] of the cause of the eczema. For this reason, all these children should also receive routine environmental control instruction. This includes dust-proofing the bedroom, application of dust-proof mattress and pillow covers, closing of hot air vents and removal of toys and other dust collectors and producers from the bedroom.

The patient must avoid chemical, inhalant or abrasive injury to his skin by means of soaps, detergents, cleaning fluids, chemicals, wools, furs, animal pets, raw foods or vegetable oleoresins or pollens.

During the acute exudative stage of eczema use of wet compresses such as Domboro soaks reduce inflammation, itching and trauma as well as remove exudate. Colloidal baths such as starch or oatmeal are absorptive, cleansing and antipruritic. Itching may be further reduced by oral administration of elixir of Benadryl, 1-3 teaspoonfuls q. 4. hr., prn, or syrup of Atarax (½-1½ teasp. b.i.d. and H.S.). One should avoid excessive sweating and heating, as this increases itching.

During the acute state generally lotions are preferable to ointments.

One of the most useful ointments for the local treatment of eczema in the subacute phase is the so-called "1-2-3" ointment:

Burrow's solution	10.00
Anhydrous lanalin	20.00
Lassar's paste	30.00

To this one may add such items as Vioform, 1-3 per cent, hydrocortisone, ¼-2.5 per cent. Phenol, 0.5 per cent is often added for its antipruritic effect. One to three per cent liquor carbonis detergens in "1-2-3" ointment is also helpful in chronic eczema. Generally, local ointments work better if bandaged on or wrapped with Saran Wrap. Signs of secondary impetiginization require systemic antibiotics.

The patient's underclothing and bedding should be washed in a chemically neutral cleanser such as "Safe Suds" or powdered "Vel."

Occasionally, systemic steroids may be used for temporary relief, especially to clear the skin for skin testing. It should never be used in lieu of good general pediatric, allergic or dematologic care.

4. *Criteria for skin testing.* If a combination of symptomatic medication, environmental controls, and an elimination diet fail to keep eczema under control, or if a major respiratory allergy develops, allergy skin testing should be carried out. When any skin testing is done, scratch tests should be done first with those food and inhalant allergens to which the child's history suggests he is frequently exposed. Intradermal testing should be done only with the inhalant allergens to which the child did not react on scratch testing. Those items to which the child is thought to be extremely sensitive clinically should NOT be used in testing. The patient should be warned to take no antihistamine or sympathomimetic medicines at least twelve hours before testing.

5. *Hyposensitization therapy.* If the items giving positive skin tests can be avoided, no hyposensitization therapy is indicated. If not, however, specific hyposensitization therapy should be started, using the inhalant allergens to which the patient's history and/or skin testing suggest he is sensitive. Since hyposensitization injections have been known to flare the patient's eczema, the initial injections should consist of extremely dilute solutions, such as 0.01 ml. of a 1:1,000,000, weight by volume, dilution of the inhalant antigens used. No good statistical studies on the value of hyposensitization in atopic eczema are available. Tuft[10] has presented documentation that hyposensitization with house dust components are occasionally quite beneficial for eczema. Pollens and molds are also known to cause eczema. If improvement in the clinical condition does not ensue within a year's hyposensitization therapy, one probably cannot expect improvement from this form of therapy alone.

Hay Fever

1. *Natural history.* Pollenosis to tree, grass or weed pollens may occur at any age. It commonly begins in children first between the ages of two to five years. In the first year in which symptoms occur they may be very mild, consisting of watering and itching of the eyes, nose and throat or ears. Varying degrees of sneezing and nasal stuffiness may occur. Symptoms frequently increase in severity with each successive year after their first appearance. They are usually worse at night because of the dew-like settling effect of the pollen, because of the occurrence of down-drafts of air currents at night, and because of the new day's supply of pollen released into the air in the early morning hours. Symptoms should be temporarily reduced during a heavy rain. A few children will also develop atopic eczema or vaginitis in the pollen season. Some will have a temporary loss of hearing.

2. *Prophylactic measures.* Because of the tendency for young patients with hay fever to develop asthma[11] first in the pollen season and then perennially, early specific hyposensitization therapy is highly recommended even for mild symptoms. In a controlled clinical study[12] in Rochester, N.Y., none of those hay fever patients receiving hyposensitization therapy developed pollen asthma, compared to a fifty per cent incidence of developing asthma in a control group who received only symptomatic medication.

3. *Symptomatic management.* For patients with moderately severe hay fever an air filter or air conditioner should be used to filter the pollen from the air in the patient's bedroom. Since the concentration of pollen in the outdoor air is usually greatest at night, this reduction in exposure to pollen by some type of air filter will make the patient much more comfortable. Any device used should have as its basic principle the delivery to the patient's bedroom of fresh outdoor air, essentially filtered free of pollen and mold spores.

Where it is feasible for a patient to spend a major part of a pollen season in an area of relatively low pollen concentration, this is desirable.

To lessen itching, watering eyes installation of eye drops which contain epinephrine or ephedrine (e.g. Wyeth's Collyrium and ephedrine), antihistamine (e.g. Ciba's Antistine), or extract of rose petals (Estavin) are usually helpful.

For relief of nasal symptoms, oral antihistamines with or without nasal decongestants are usually helpful. Except in extreme situations oral or parenteral steroids should not be used in the treatment of pollenosis uncomplicated by asthma.

4. *Criteria for skin testing.* Any child with symptoms suggestive of grass or ragweed pollenosis which recurs a second season or which is accompanied by wheezing should be skin tested with summer pollen and mold spore extracts.

5. *Specific hyposensitization therapy.* In children with a history of grass or ragweed pollenosis and a positive skin test for ragweed or timothy, regardless of the severity of their symptoms, hyposensitization therapy is indicated. Allergens to be used in injection therapy should include those pollen and/or mold spore allergens which the patient's history and skin testing suggest are important to his disease. Injections should be started well in advance of the pollen season in order to attain adequate dosage before the pollen season begins. Unless one has had experience in individualizing dosages in many such patients, one should begin hyposensitization injections with an extremely small dose such as 0.01 ml. of a 1:500,000 dilution of pollen extract. The concentration of some extracts is expressed as P.N.U., protein nitrogen units, or as Noon units. The equivalents for these units are shown in Table I.

Table I

Comparison of Unit Values of Pollen Extracts in 1 ml.

Weight per Volume	*Milligrams Total Nitrogen*	*Protein Nitrogen Units*	*Noon Units*
1:1,000,000	.000013	0.6	1
1:100,000	.00013	6.0	10
1:10,000	.0013	60.0	100
1:1,000	.013	600.0	1000
		6000.0	10000

The injections should be given twice weekly until the maximum tolerated dose is reached. Thereafter the injections may be given at three to four week intervals the year round. During the pollen season the injections may be given temporarily once or twice weekly, if the patient is having enough symptoms to be uncomfortable. He should ALWAYS remain in the doctor's office at least thirty minutes. If he develops any sign of a generalized reaction, such as hives, wheezing, cough, or itching in the palms or throat, the patient should be given 0.20 ml. of aqueous 1:1000 epinephrine subcutaneously into the site of the pollen injection.

The dose of the pollen injection is increased by 0.10 ml. of a given dilution until a dose of 0.50 ml. is reached. Then 0.10 ml. of the next dilution is given at the next visit. This regime is followed until the patient reaches a pollen dose of 0.30 ml. of approximately a 1:200-1:500 dilution (1200-3000 P.N.U.), or the highest dose which a patient can tolerate without a generalized reaction, whichever is smaller. For some patients the dose may have to be reduced during the pollen season because of mild reactions to a dose which the patient can tolerate outside the pollen season. If mold spores or other antigens are being given along with pollens, the dose of these other antigens should not exceed a concentration of 1:5000.

Unless one feels perfectly comfortable about doing this, it is generally safer for a physician to have someone trained in allergy to prepare the individual injection mixture, tailored to the patient's need. The administration of the injections can then be carried out in the office of the referring physician. Whenever practical, it should be the goal of the allergist to return the patient to the referring physician as soon as possible, so that the patient will be essentially under his own physician's care throughout his treatment.

Hyposensitization therapy should be continued until the patient has gone a whole year essentially free of hay fever and asthma. This may mean that he will have to take injections for an indefinite period of time.

Bronchial Asthma

1. *Natural history.* Asthma is an allergic pulmonary disorder characterized by recurrent attacks of obstructive emphysema involving both lungs throughout, and with paroxysms of an expiratory type of dyspnea and wheezing. The wheezing should be best heard with the stethescope placed on the chest wall, whether or not one can hear it with the unaided ear. It should be relieved, at least partially, by epinephrine. The symptoms may occur at first sporadically and be so mild that no wheezing can be heard except with the help of a stethescope. It may begin as an intermittent cough, followed days, weeks, or months later by classical wheezing. It may begin as spontaneous severe dyspnea and audible wheezing. It uncommonly begins sooner than six months of age. In childhood it usually begins before six or eight years of age, but it may begin at any age. The etiological allergens may include foods, pollens, molds, animal danders, drugs and chemicals. Once it has become established, it may be triggered off by nonspecific stimuli such as infection, exertion, fatigue, extremes of temperature, strong odors and emotional factors. It is the exception rather than the rule for it to be spontaneously "outgrown."

2. *Prophylactic measures.* Of the children with perennial asthma seen in the pediatric clinic at Strong Memorial Hospital in Rochester between 1951-58, approximately eighty per cent had had preceding pollenosis. Consequently, we feel that one of the most important prophylactic measures in preventing asthma in childhood is early hyposensitization therapy for even mild ragweed pollenosis.

Since measles may trigger an initial asthma attack in a potentially allergic child, all such youngsters should be actively or passively immunized against measles if they have not already had the disease. In addition, because pollenosis or pollen asthma is often followed by winter asthma or perennial allergic rhinitis caused by indoor inhalable allergens, patients with these conditions should have general dust-proofing measures instituted. They should have dust-proof covers on their mattresses and pillows. Live furry pets should be kept from their bedrooms and preferably out of the house entirely. If any kind of mild winter inhalable allergies develop, even more rigid environmental controls should be recommended. Hot air registers should be closed and an alternative source of heat should be provided. Swineford[13] has stressed the importance of treating asthmatics when they are in the early stages of paroxysmal attacks. In this stage, ninety per cent obtain satisfactory relief, whereas only about one half or less of adult asthmatics in the chronic stage are satisfactorily relieved.

Parents should be urged to give symptomatic medicines at the first sign of symptoms rather than waiting until the symptoms are well established. This may abort an attack at its inception.

3. *Symptomatic management.* Parents should be encouraged to try new symptomatic medicines when the child is well, in order to determine whether it agrees with the patient. They should keep a drug diary with four columns: (1) names of the medicine, (2) purpose of the medicine, (3) any side effects or idiosyncrasies, and (4) effectiveness of the drug. Prescription should be labelled so the patient or his parents will be able to report on effectiveness or side effects of a particular medication.

Sympathomimetic drugs are the most commonly helpful medications for asthmatic symptoms. Epinephrine HCl, 1:1000 given in a dose of 0.15-0.30 ml. subcutaneously is the drug of choice. It may be repeated once in twenty minutes and then at four hour intervals, if needed. The dose of the longer acting epinephrine, Susphrine-glycerine suspension of epinephrine crystals, 1:200, is 0.15-0.25 ml. Aminophyllin may be given by vein, rectum or mouth. The rectal dose should not exceed 7 mg/kg in children and should not be repeated sooner than six to eight hours after the initial dose. If given by mouth, the dose should not exceed four mg/kg t.i.d. Combinations of ephedrine, theophylline and phenobarbital are available as tablets or liquids. Liquefaction of secretions may be accomplished by giving saturated solution of potassium iodide in a dose of 5-15 drops, t.i.d., p.c. in juice or milk. To facilitate the action of this medication the patient should be urged to drink a lot of fluids.

If evidence of bacterial infection exists, antibiotics are indicated. Otherwise, they are not.

Isoproterenol is available for use in a hand nebulizer, as an elixir and as a sublingual glosset.

In spite of some recent published articles to the contrary, injections of gamma globulin have not been shown to be effective in the control of bronchial asthma.

One factor leading to the unnecessary use of antibiotics and gamma globulin has been the failure in studying young wheezing patients to rule out such conditions as hypogamma globulinemia, tuberculosis, cystic fibrosis of the pancreas and foreign body in the lung. Every child with wheezing associated with infections probably deserves to have a chest x-ray, a Schick test, and a tuberculin test. In some patients a barium swallow under fluoroscopy, a sweat chloride test and an immunoelectrophoresis of the serum should be performed.

Usefulness of antihistamines in asthma is said to be limited and perhaps harmful because of their drying effect on the mucous membranes. In infants and young children, however, asthma attacks are sometimes aborted, prevented or stopped by administering antihistamines.

Sedatives are often necessary to allay apprehension. Spiritus frumenti (one teaspoonful per twenty-five pounds of body weight in two or three ounces of ginger ale or "coke"), syrup of atarax (½-1½ teaspoonfuls at bedtime) or a short-acting sedative such as secobarbital or chloral hydrate are often helpful for this purpose.

Although many allergists feel that the prime indication for prescribing steroids is status asthmaticus, it is occasionally useful in preventing status. Needless to say, cortisone and its derivatives are two-edged swords. Every physician using them bears the responsibility for protecting his patient from the possible harmful side effects of these medicines. Steroids should never be used purely as a symptomatic crutch in lieu of a more definitive allergy study on a patient. Every effort should be made to avoid long term use of steroids, especially in growing children.

Since children and adults in status asthmaticus are often suffering from dehydration and acidosis, intravenous fluids are nearly always indicated.

4. *Criteria for skin testing.* Infants with asthma should first have a trial of an elimination diet as described for patients with eczema. Unlike adults and older children infants with asthma may be dramatically helped by dietary restrictions. At any age, if dietary manipulation, symptomatic medicines and environmental controls do not easily and completely control the asthma, skin testing should be done as in the case of eczema. One should choose antigens to be tested judiciously after a careful review of the history and physical examination of the patient.

5. *Specific hyposensitization.* If avoidance of allergens to which the patient reacts on skin testing is impossible, impractical or not helpful, hyposensitization with air-borne inhalant allergens should be started. An injection schedule similar to that described for pollenosis should be followed. When the patient reaches his highest tolerated dose, this dose should then be given every one to four weeks. If the patient is doing well, he may go four weeks between injections. If he develops symptoms regularly in the fourth week after injections, he should take them every two to three weeks. There is no objection to giving hyposensitization injections to a child with an afebrile "cold" after he has reached his stabilized top dose. He should continue taking the injections until he has gone a whole year free of wheezing. The value of this type of treatment has been verified in a controlled clinical study[14] in the pediatric allergy clinic of the Strong Memorial Hospital.

Perennial Allergic Rhinitis

1. *Natural history.* This is the commonest of the major allergic syndromes known to man. It is characterized by pallor and edema of the nasal membranes. This may result in nasal obstruction, with resulting snoring, mouth-breathing, morning sore throat and itching of the nose. It may cause the characteristic watery nasal discharge, rich in eosinophils. It may drain out anteriorly, causing a chronic or intermittent "running nose" or repatitive sneezing. It may drain posteriorly and produce the classic "post nasal drip." A common problem for patients and physicians alike is to be certain that the presenting symptoms are of an allergic nature. His symptoms may mimic the common cold or bacterial infections of the nose, sinuses, adenoids, ears or throat. Infants often cough or repeatedly clear their throat or snort. Because the combination of mucus secretion and obstruction predispose to bacterial infection, such infections often confuse the clinical picture and blind the physician to the basic underlying cause of the patient's symptoms. This is especially true in the case of repeated bouts of sinusitis in adults or ear infections in children. One of the most distressing symptoms it may cause in young children and adults alike is obstruction of the openings of the eustachian tube. This may result in frequent ear infections or the accumulation of sterile clear fluid in the middle ear. Szanton and Szanton[15] have called attention to the fact that children with perennial allergic rhinitis may develop transient hearing loss. This cause of deafness is often overlooked by school doctors and pediatricians. Its presence in the absence of nerve deafness or ear drum trauma should by itself suggest the diagnosis of allergic rhinitis.

Perennial allergic rhinitis may occur at almost any age. Between the ages of 3-12 months food allergy alone may be the cause. Thereafter sensitivity to inhalant allergens such as dust, molds, animal danders, drugs, and pollens become more important causes. Some of these children and adults will ultimately develop polyps, sinusitis and/or asthma.

2. *Prophylactic measures.* The prophylactic measures recommended for eczema may lessen the likelihood of developing allergic rhinitis. Environmental controls to lessen exposure to dust, fumes, animal dander, molds and pollens lessen the likelihood of developing this condition. This is well documented in the case of war brides who came to this country and then for the first time became exposed to high concentrations of ragweed pollen as well as indoor dust-borne antigens circulated by hot air heating systems. Many of these people who had no knowledge of a hereditary predisposition to allergic disease, subsequently developed pollenosis, asthma or perennial allergic rhinitis. Their symptoms usually promptly subsided during a return trip to their homeland.

Low humidity not only dries out mucous membranes of the respiratory tract, but also increases the bouyancy and circulation of airborne allergens. The relative humidity of the bedroom should be kept between 40-60 per cent. Maintenance of proper humidity together with the closing of hot air registers in bedrooms may help prevent the development of perennial allergic rhinitis in potentially allergic individuals.

3. *Symptomatic management.* If examination of the nasal smear or of a peripheral white blood count suggests the presence of a secondary bacterial infection, antibiotics are indicated. Topical rhinologic therapy is helpful in the initial phase of treatment. Some nose drops, however, produce secondary vasocongestion and so should be avoided. Neosynephrine 0.25 per cent is a satisfactory nose drop. Nasal polyps may have to be surgically removed to help improve nasal ventilation and promote nasal drainage.

Antihistamines alone or together with nasal decongestants are often helpful.

The patient should be instructed to avoid chilling, especially at night. His bedroom temperature should fall below 70°F. Wearing a hat out of doors in inclement weather as well as wearing a "nightcap" are often helpful.

Steroids, while dramatically helpful, should be used in only exceptionally severe cases and then in minimal doses for a short period.

4. *Criteria for skin testing.* Many patients with this condition are only minimally bothered by their symptoms, which are easily controlled by a combination of environmental controls and symptomatic medications. If a patient with perennial allergic rhinitis persists, in spite of the above measures, with mouth breathing, hearing difficulty and/or repeated ear infections (especially if he has already had an adenoidectomy), he deserves further allergic study.

5. *Specific hyposensitization therapy.* Some patients with perennial allergic rhinitis will improve with dietary restrictions or avoidance of other allergens suggested by the history or skin test results. If, however, these measures fail to bring relief of symptoms, specific hyposensitization with suspected inhalable allergens is in order. If house dust is a major offending allergen, the inclusion in a patient's injection materials of an extract prepared from his own household dust may be helpful. An injection schedule similar to that described previously will suffice.

If a patient's symptoms suggest the need for an adenoidectomy, this procedure should be done preferably in the non-pollen season and only after careful allergic study and management has been instituted.

Finally, there are certain general points on prevention and treatment of allergic symptoms in allergic patients.

Prevention

1. Whenever possible avoid injection of penicillin. Always ask about any previous reactions, if it must be given this way.

2. All patients in whom an insect sting is followed by fainting, generalized hives, headache, joint pains or wheezing should be hyposensitized.

3. Before administration of vaccines grown in check embryos, check for history of egg allergy. If in doubt, do a scratch test with a 1:100 dilution of the vaccine.

4. Take seriously any history of a severe generalized reaction to a food or drug.

5. Before doing intradermal tests with allergy extracts, do preliminary scratch tests. Never test with an item where a reliable clear cut history of a generalized reaction to this item exists.

6. Before giving horse or bovine serum by injection, always do a preliminary scratch test. Take every opportunity to advise adequate active immunization with tetanus toxoid to lessen the need for horse serum injections. Tell patients or parents the difference between toxoid and antitoxin.

7. If a patient has a generalized reaction to a hyposensitization injection, the dose of any further injections of the same material must be reduced.

8. Keep aqueous epinephrine and oxygen always on hand.

Treatment Of Allergic Emergency

1. Have the patient lie down. Inject 0.10 to 0.40 ml. of aqueous epinephrine subcutaneously or intramuscularly.

2. If it is known that a drug injection or insect sting caused the reaction, inject an additional 0.10 ml. of aqueous epinephrine into the site of the injection or sting. If the lesion is in an extremity, place a tourniquet above the site, releasing it cautiously and intermittently.

3. Although antihistamines and steroids by mouth or injections may give some relief of symptoms, if the patient survives, epinephrine should be the first medicine given.

4. Oxygen inhalation may combat anoxia. Artificial respiration or intermittent positive pressure may also help, if the patient is cyanotic or in shock.

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Cardiology

It was not until the eighteenth century, with the publication of observations on morbid anatomy made by Raymond Vieussens (1715), Lancisi (1718, 1740), and Morgagni (1761), and the first treatise dealing specially with diseases of the heart by J. B. de Senac (1749), that cardiac disease was really recognized. Theophilus Bonetus (1620-89), in the first volume of his *Sepulchretum* (1679), collected a number of observations on palpitation and cardiac pain during life associated with polypi in the heart, calculi in the myocardium, inflammation of the heart, acute inflammation, effusion and adhesion of the pericardium, and aortic aneurysm, and thus prepared the way for Morgagni and others. Sir Humphry Davy Rolleston.—*The Harveian Oration*. Great Britain, Cambridge University Press, 1928, p. 13.

Liver Trauma And Delayed Massive Hemobilia

G. S. Parrella, M.D.

■ In May 1848[8] a twenty-two year old male of the sporting type was engaged in a carriage race through the streets of London when he was accidentally thrown from the vehicle. Over the next eleven days this patient developed repeated bouts of abdominal pain, collapse, jaundice and bloody stools. He finally died of his mysterious illness. At autopsy there was a large laceration in the dome of the liver which undoubtedly had fed blood into the biliary tract and thus into the duodenum. As far as is known this is the first recorded case in medical literature of massive hemobilia following blunt trauma to the liver. Although our means of transportation have increased in velocity and the accidents have increased in violence, there have been very few reported cases of massive hemobilia in the literature since that time. In 1961 Spencer, Menguy and Eiseman could find only nineteen cases of hemobilia with a mortality of approximately 50 per cent.[13]

Crosthwait and co-workers reported that the mortality following blunt trauma to the liver was 44.8 per cent.[2] Mikesky, Howard and DeBakey[7] in their extensive review article in 1956 reviewed three hundred cases of liver trauma and stated that the mortality in non-missile injuries was as high as 71 per cent. Ten out of the three hundred cases had recurrent delayed hemorrhage. Only one had hemobilia and this fortunately subsided spontaneously without treatment.

Report Of A Case

This is a twenty-one year old male who was admitted to Milford Hospital on October 20, 1962 complaining of abdominal pain. One week before admission he drove into a tree while trying to avoid a dog crossing the road. He was taken to another hospital in the area, examined in the accident room and discharged. A day later he came to the Milford Hospital Emergency Room where X-rays of the abdomen and chest were taken. After a blood count was done he was discharged. However, he continued to have intermittent bouts of abdominal pain and vomiting at home. On the day of admission he developed very severe right-sided abdominal and chest pain together with severe backache. Physical examination revealed right upper quadrant tenderness and the patient was admitted to the hospital. The next morning the pain was gone but the hematocrit continued to drop slowly and he was transfused. He ran an intermittent febrile course. On the fifth hospital day a surgical consultation was requested. Examination revealed a very tender mass, approximately 3″ in diameter, in the right subcostal area which moved with respirations. A preoperative diagnosis of ruptured liver with hematoma was made. At operation the mass was found to be the gallbladder distended with blood clots and bile. High on the dome of the right lobe of the liver were stellate lacerations, the longest being about 6″ in length and the others 2″ to 3″ long. There was bile and blood in the abdominal cavity. The lacerations were not actively bleeding at this time and were closed with difficulty because of their location. Mass ligatures were used over surgicel® packs. A cholecystectomy was done and the area of the liver was drained with many Penrose sheaths. Over the next week a large amount of bile drained from the wound and a right pleural effusion developed which responded to thoracentesis. On the tenth postoperative day he had an episode of tarry stools which did not recur and he was discharged on the twenty-seventh postoperative day. Four days later after eating a large meal he was admitted following a massive hematemesis. A GI series showed an irritable duodenal cap. The patient was treated with iced saline gastric lavage and bleeding ceased immediately, but two days later he was clinically jaundiced. This disappeared in about thirty-six hours and the patient was discharged. A day later he was re-admitted for the third time complaining of epigastric pain after a full meal. Abdominal examination showed very slight mid-epigastric tenderness without spasm. The pain subsided only to return three days later accompanied by currant jelly stools. It was decided to re-explore the liver through a thoraco-abdominal incision. The common duct was probed and bloody bile was found. A T-tube was inserted. The lacerated area of the liver was incised, old clot was evacuated and bleeding vessels in the depth of the wound were individually clamped and ligated with suture ligatures. The liver was again drained and the drains were removed on the eighth postoperative day. On the tenth postoperative day the T-tube drainage again became bloody and the patient developed severe abdominal pain and peripheral collapse. The patient was now operated on a third time. The thoracoabdominal wound was reopened and this time the right lobe of the liver with the exception of the portion immediately adjacent to the gallbladder bed was resected. The resected liver showed a large focus of complete necrosis with overlying organized and organizing blood clots. On the thirtieth postoperative day the patient was discharged and has remained well ever since.

Comment

This case is interesting first because of the difficulty with which the diagnosis was made. He was apparently examined by three other physicians prior to his first operation, all of whom felt that

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the abdominal findings were not alarming. In his exhaustive report on trauma of the liver including both civilian and war wounds, Madding collected 829 cases.[6] Only nine per cent of these were still bleeding at the time the patient was explored.

The classical sign of liver trauma is upper abdominal pain which increases on respiration and radiates to the shoulder, usually the right.[4] Nausea and vomiting are not common and tenderness and spasm may be absent if free bleeding into the peritoneal cavity does not occur. Occasionally in blunt trauma a mass appears in the right upper quadrant. This may be due to a hematoma either at the edge of the liver or between the liver and the diaphragm. It may however also be the result of distention of the gallbladder by blood entering the biliary tract. Once the decision to explore such a case has been made, arrangements should be made to replace almost the entire blood volume of the patient—namely, 4,000 to 5,000 cc's of blood should be on hand. The patient should be so placed that the incision can easily be extended into the thorax to expose the dome of the liver transdiaphragmatically.[9]

In reviewing the literature, one is struck by the frequency of delayed hemobilia when the trauma involves the right lobe of the liver with consequently only slight intraperitoneal hemorrhage. The surgeon often did not realize the extent of the laceration because of the poor exposure through a strictly abdominal approach. In large series of liver injuries the right lobe is involved twice as often as the left.[3]

Re-exploration of patients who have sustained a laceration of the liver with delayed hemobilia may not readily reveal the source of the secondary hemorrhage. There are reports in the literature where such patients have been re-explored and have had cholecystectomies, explorations of the common duct, vagotomy and pyloroplasty, drainage of a subphrenic abscess and gastrectomy without cure because the liver looked grossly normal from the surface.[11, 5, 12] Spencer, Menguy and Eiseman were able to find the source of the hemorrhage only after doing an operative cholangiogram at the time of the third exploration of their patient. In order to avoid this serious complication of liver trauma then, it is important to explore the liver at the first opportunity and to debride the wound thoroughly, resecting major portions of the liver that may be devitalized by large lacerations.

In the case reported above, gastro-intestinal hemorrhage became evident ten days after his first operation. In common with many other cases reported in the literature, it was assumed that this was due to stress ulcer. However, another clinical finding occurred which was largely ignored, that being jaundice. All who have had experience with such cases have stressed the fact that these patients have pain resembling biliary colic, have hematemesis or melena and have clinical manifestations of jaundice, probably obstructive due to clots in biliary radicles.

It should be pointed out that secondary hemobilia may very rarely occur as late as several months after the original trauma and at such times it is impossible to tell either by inspection or palpation of the liver just where the source of the hemorrhage is located. It is wise under such circumstances to try aspiration of the organ, or to do an operative cholangiogram in order to locate the obstruction or the fistula in the biliary tract in the depths of the liver. In this case the decision was first to attempt individual ligation of the bleeding vessels in the liver. The subsequent course proved that it would have been much wiser to resect the damaged portion of the liver because of the depth of the laceration and the inability to accurately oppose the wound edges with suture material.[1] The third operation finally resulted in a cure of this patient and demonstrates what is probably the best type of management of large contused lacerations of the liver resulting from blunt trauma, namely debridement and resection.

Secondary hemorrhage following liver trauma may not always be as dramatic as in the case cited above. Bouts of abdominal pain following recovery from liver injury may escape diagnosis but may well be due to fresh bleeding from old liver wounds into the biliary duct system. Such patients should be studied for subclinical jaundice and/or occult blood in the stool. From a personal small collection of liver trauma cases we have seen at least one patient who may have had delayed pain due to recurrent hemorrhage which however subsided spontaneously.

The technique of liver resection is adequately discussed in the literature and will not be entered into here except to say that temporary clamping of the blood supply at the hilus of the liver is sometimes helpful although it must be remembered that 15 minutes is about all the anoxia that the liver will safely tolerate.[10]

Conclusions

1. The majority of delayed hemorrhage of liver trauma occurs in lacerations of the right lobe of the liver. 2. The gallbladder is always distended with blood and is palpable at some time during the course of the illness. 3. The pain is episodic and suggests biliary colic. It is almost always associated with shock, jaundice, melena or hematemesis and usually with spiking fever. 4. Bleeding usually follows ingestion of large amounts of food. 5. Drain-

age procedures on the gallbladder or ducts are insufficient to prevent the recurrence of massive hemobilia. Packing of wounds with hemostatic agents might probably favor the occurrence of late secondary hemorrhage by introducing foreign material and clots between the opposing edges of liver lacerations. 6. Resection is advised only for major contused liver lacerations and a thoraco-abdominal incision is the approach of choice. 7. It may be very difficult to see or palpate any pathology in the liver at the time of secondary exploration. Needle aspiration or cholangiography may be helpful. 8. Gastrointestinal hemorrhage from old lacerations of the liver or massive hemobilia may be a frequently undiagnosed sequel to automobile accidents and even an undiagnosed cause of death.

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Background

Whoever then devotes himself to his useful study and would make the greatest advantage of this short life in the pursuit of so extensive an art, should first take a view of its rise and progress and present state. But, I should premise, he is supposed to come to this study sufficiently versed in Latin and Greek and able to read over one or two modern languages. And though his character as a scholar (for every physician is expected to be such) besides his acquaintance with the ancient classical writers, requires that he should not be ignorant of geography, chronology, history, logic, metaphysics, ethics, mathematics and natural philosophy; yet of all these the two last demand his especial attention, if he would be secure from error, and superstition, from mistaken theories and ill grounded practice. Thus prepared then let him take a general survey of the ancient and present state of physic.—William Heberden. *An Introduction to the Study of Physic.* New York, Paul B. Hoeber, Inc., 1929, p. 77.

The Five-Day Program To Help Individuals Stop Smoking

A Preliminary Report

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■ Any program that offers help to the chronically addicted tobacco user is of importance these days when there is ever increasing evidence that the use of tobacco is a definite health hazard. It is not the purpose of this paper to make an exhaustive study of these facts, but rather to give a preliminary report of a program designed to help the tobacco user overcome his habit. We shall discuss the methods of what is done during the Five-Day Program and a preliminary evaluation of results.

For the past three years two of us (JWMcF and EJF) have been conducting group-therapy sessions combined with a physical fitness program for the chronic adult smokers, most of whom have tried to quit before, but have found it difficult or impossible. About forty such group-therapy sessions have been held in cities throughout the United States and Canada. At the present time we are training other teams to conduct these group-therapy sessions.

The Problem

In evaluating and attacking the problem of tobacco addiction, a word regarding the nature and scope of this almost universal habit is in order. Smoking, being a very complex neuromuscular habit, has psychological, physiological and social components that make it one of the most deep-seated habits.

Recent studies are beginning to show something of the magnitude of this problem in both the United States and Canada. Opstad[1] estimates that deaths from cancer of the lung, coronary heart disease, and emphysema, in which smoking plays a major factor, are between 94,823 and 100,000 per year in the United States. Horn[2] states that "there would be somewhere in the neighborhood of 300,000 to 500,000 fewer deaths per year if it were not for smoking. . . . it represents about one-sixth of the 1.8 million deaths which we have in this country. (U.S.A.) Not that these deaths would not occur . . . but they would occur later."

The epidemiological data of deaths in Ontario, Canada; the United States; England; and Wales, summarized by Delarue,[3] and the study by Best, Josie and Walker[4] of the Canadian Department of National Health and Welfare all show the correlation of smoking and crippling lung diseases, especially cancer of the lung. Twenty per cent of cancer deaths in North American males are due to cancer of the lung, and the death rate from lung cancer among those who smoke twenty or more cigarettes is fifty times that of the non-smoker.[5]

The concern of governments, health agencies, and medical circles attest to the fact that here is a major health problem that will require and test the ingenuity of all concerned in bringing not only the facts before the public, but assisting and helping those individuals who desire to stop using tobacco.

Programs By Others

A strong educational program is being promoted by both the American and Canadian Cancer Societies to enlighten adults and especially youth on the hazards of smoking. The American Heart and T.B. Association is also carrying forward a program of giving the facts on tobacco to the public, and to prevent youngsters from starting the habit. Dr. Ejrup[7a,b] of Stockholm, Sweden, now conducting a study at New York Hospital, New York City, has

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had one of the largest clinics. He uses a combination of medication and psychotherapy. The same methods are in use by Rosenberg[8] in Denmark's tobacco withdrawal clinic. Lawton[6] has endeavored, through a group therapy approach, to help adults in giving up cigarettes. Moore and the group of workers[9] at Roswell Park Memorial Institute, Buffalo, New York, have launched a clinic to help people stop smoking. In all of these studies it is evident that not all the answers are in as to the best way of helping the smoker to stop. Ejrup's[7c] figures of 50 per cent staying off the tobacco for six months after an initial 75.8 per cent had stopped among 1,000 cases is impressive. However, all workers stress the need of a follow-up program for maximum effectiveness. This has been our experience as well.

It soon becomes apparent to anyone who has tried to help a group of individuals to give up tobacco that facts alone on the health hazards of smoking are not enough. Among lung cancer research scientists from all over the world, Lawton and Goldman[10] discovered that 30 per cent are still smoking, although 83 per cent of them believe there is a definite relationship between smoking and lung cancer.

The Development Of The Five-Day Plan

While working in a peripheral vascular clinic in the early 40's, one of us (JWMcF) noted that many a man with Buerger's Disease would look helpless when told by his physician he must give up cigarettes. "I can't quit, doc," was a common expression of these sufferers from Buerger's. It didn't seem right to ask a man to stop something and not give him some sort of help when his limbs and even his life were at stake. A start was then made and a program has gradually developed through the intervening years. At first this was done with the single patient.

In 1959, JWMcF[11] reported a ten-day program used among individuals who wished to stop smoking. This had proved quite effective with small groups of 15 to 30 individuals in New York City and with individual patients at the Battle Creek Health Center, Battle Creek, Michigan.

Since the summer of 1960, we have had an opportunity to enlarge the scope of the program and its effectiveness. It was then that EJF, a clergyman, proposed that a shorter period of time be tried—a five-day period. He had helped many individuals to stop smoking and was much interested in the psychological problems involved. We joined forces and soon discovered that with both of us working together it was possible to reduce the number of days required for the basic instruction from ten to five. We also discovered that you could have groups of three hundred or more and still be effective in helping the individual stop smoking.

Other factors which we have kept in mind in developing our Five-Day Program have been the nature of nicotine itself. It is an addictive drug, producing first stimulation, then sedation of both the autonomic nervous system and the central nervous system.[12] In addition to this there can be physiological and psychological addiction or a combination of both in many smokers.[13] We cannot overlook the social dynamics[14] that also exist in the continuation of this habit. The habit of smoking obviously requires the use of many disciplines, for the total man is involved, not just his reaction to nicotine alone.

We have used a physician-clergyman team in all our lectures and group therapy sessions. This approach appears to have succeeded in helping many a chronic smoker who has tried to quit before but has been unsuccessful; besides, the presentation, by a man of the cloth, of the emotional and psychological problems involved does have an impact on the individual that often the physician alone cannot give. We would hasten to add that this is not a religious program of teaching creed, or dogma of any type. It is strictly a preventive medicine measure sponsored by the medical department of our church organization, and rendered as a community service.

Mechanics Of Group Therapy Sessions

Five evenings of one and one-half to two-hour sessions are held beginning on Sunday and running through and including Thursday evening. A follow-up meeting is arranged for the first of the next week to determine how well the new non-smokers are making out.

These classes are held in a convenient auditorium of a school, large hotel, or civic hall. The meetings are announced the week before at civic clubs, community health agencies, medical groups, over radio, television and through the public press.

These sessions are a combination of lectures, films and demonstrations with question and answer periods each evening on the tobacco problem. Specimens of lung cancer are displayed.

Cooperation Of Other Agencies

There is excellent literature available through the American and Canadian Cancer Societies and also the American Heart and T.B. Association. At the recent meeting in Calgary, posters, brochures and films were used which were produced by the Canadian Cancer Society. The cooperation of city health officials and local physicians was incorporated by a lecture on emphysema and other crippling lung diseases. (WAJD and HWG)

Areas Covered By Group Therapy Sessions

Since it is known that any addictive drug has ramifications into practically every phase of living, and since what appeals and will help one person may not benefit another in the least, we try to give the tobacco addict all-out support in every facet of his life. Physically, mentally, morally, and socially, he will need help. For this reason we put him on a good health and physical fitness program; help him with better motives than fear to stop his smoking; show him how to meet social pressures and to obtain strength through a firm conviction of a Power greater than himself. Soon habit patterns that were associated with smoking are substituted with good health habits.

Following are the pertinent points covered during the group therapy sessions in the physical, mental, spiritual and social areas of the tobacco user:

Physical Or Physiological Aspects Of Program

We prefer the sudden cessation and complete withdrawal of all tobacco. This we feel is easier in the long run than snipping away at this habit for weeks or months on end.

1. During the first 24-hour period, we "force fluids"—six to eight or more glasses of water between meals. We also use hydrotherapy—warm or neutral baths, hot and cold showers, or cold mitten friction baths that can be carried out at home; the warm or neutral baths at night; the tonic measures, such as hot and cold showers, in the morning.

2. Except for the first 24-hour period, when he is encouraged to eat largely of fruit, the individual is placed on a bland, low cholesterol diet. All alcoholic and caffeine-containing beverages are eliminated, as well as highly spiced foods. We soon learned with many individuals, that several cups of coffee call for a cigarette. We encourage fruit for desserts, rather than rich and high-calorie cakes, pies, and ice cream.

3. A physical fitness regimen of exercise—daily walking is instituted. We do not allow these folks to sit down after meals. The urge to smoke is often then the greatest. Outdoor walking and breathing deeply for ten to fifteen minutes after eating is a "must." Slow, rhythmic deep breathing is encouraged when an overpowering urge strikes, along with a glass of water.

4. We urge the individual to avoid smoking companions, and any unusual tensions, if at all possible. He is urged to cancel night appointments to be sure of getting adequate sleep during this five-day period.

5. A daily personal control booklet, outlining what he is to do each day, is provided every student. It gives him something to do practically every waking moment. In short, he is regimented on a very strict program, and seems to thrive on it.

6. If any untoward physical signs or symptoms develop (such as binding of fluid, gastric irritation due to sensitivity to citrus fruits, or extreme nervousness), the individual is referred to his family physician with a phone call from one of us on the team.

Mental Or Psychological Aspects Of Program

1. The first evening a film is used, showing the surgical removal of a cancerous lung. This, we are free to admit, is real shock therapy—but it is effective. From this point on, we have their undivided attention on "how to stop."

2. Each evening is divided between a discussion of the psychological and physiological problems involved. E.J.F. discusses the power of choice, the proper use of the will, how to strengthen will power, and the value of concentration. Psychosomatic relationship and the complex nature of man are set forth.

3. The principles of group therapy and group dynamics are freely used. Everyone has an opportunity to get in on the act. They report on how they are getting along and are encouraged to tell of their failures, as well as their successes. Questions on withdrawal symptoms are answered.

4. How to cope with the "irresistible urge"—how to meet the problem after the five days are over—better motives than economics, or *fear* of cancer, for stopping and staying off tobacco—are freely discussed.

Spiritual Aspects Of Program

1. This is not a religious program. No doctrine, creed, or dogma of a theological nature is given.

2. We do, however, make no apology for belief in a Power greater than man. We suggest that if they have never prayed before, this is the time to begin. Some of them are going to need all the help they can get. Furthermore, we believe that an overruling Providence will come to the aid of a man or woman who is really serious about stopping the use of tobacco. The Holy Scriptures states, "Ask, and it shall be given you."[15]

3. This part of the program is similar to Alcoholics Anonymous. We stress that divine aid is a very personal thing; but when the individual has a strong craving, if he uses this aid, he will discover a very real and powerful factor in keeping up his resolve to stop smoking.

Social Aspects Of Program

We are certain that being together in a group is another strong factor in helping these individuals. The sessions after the first evening take on more the atmosphere of a classroom and a workshop with informal group participation. Even in our larger groups (200-400 or more) we try to keep an informal atmosphere. The principles of group therapy and group dynamics are freely used. From the third to the fifth evening, the students are encouraged to relate how they made out in the past 24-hour period. The discovery that others are having muscle twitching, cold sweaty hands, spots before their eyes, headache, the "jitters," mental haziness, fatigue, or other symptoms, is a big boost to all participants. When they begin to report a return of the sense of smell or taste, a sudden "clearing of their mind," or craving lessened, enthusiasm mounts. A question and answer period is a "must" for a successful session.

A "buddy system" is instituted the first evening. We feel it vital to have one partner telephone or check on the other in the morning; and in the afternoon, then reverse the process. This has helped many a person who was on the brink of breaking over.

Medication

Because of the medical ethics involved, and since our program has been of a public health and community service nature, we have not prescribed medication. We are now persuaded that with many individuals it is not necessary.

We have no objection to the individual's trying or using any of the "helps" or "tobacco cures" on the market. We have found many who state, "I've tried 'em all, doc. They didn't work."

In this connection, it is interesting to note that Rosenberg[8] in Denmark no longer uses lobeline; he feels his results have not suffered. He does use a tranquilizer.

In our own groups, we refer the extremely nervous individuals to their family physicians if tranquilizers seem necessary.

Example Of First Evening Session

So the reader can better picture what happens, we shall give in more detail what is covered on the first evening since it is typical of the procedure used in the subsequent group therapy sessions. We start with a color motion picture called "One In 20,000"*—a picture of a young newspaper editor's successful fight against lung cancer. This is a documentary film as far as the surgical scenes and the removal of the lung are concerned. Dr. Alton Ochsner of Tulane University is the surgeon in the film. We make no apologies for showing it, even though it is pretty strong medicine for some. The fear of cancer and knowing that a serious operation faces them certainly rivets the attention of the group on step two,—"What do I do to stop and avoid this thing?"

E.J.F. discusses the proper use of the will, what it is, and how to reinforce their decision not to smoke during the first 24-hour period.

From the psychological we switch to the physiological aspects of the problem. The anatomy and physiology of the lung, the effect of tobacco tar on the system and the production of lung cancer is discussed. (JWMcF) The effect of nicotine on the nervous system is presented. We then launch into a physical fitness program and how to reduce the craving for cigarettes.

They are taught the value of adequate fluids. And they keep a record of their fluid intake. The value of deep rhythmic breathing is demonstrated, and they are given deep breathing exercises to be carried out three times daily at home. We are not against having a bit of humor now and then. We tell them this is the time to go on a "fruitjag"—unfermented of course! We point out that alcohol can be a real booby trap. They must remain simon-pure for these five days.

Their diet is liberalized following the first day, but if some cannot make it through the first day, we have a menu for them to follow. The menu is found in the control booklet, which is next handed out. Time is then given for questions and answers, following which they are paired in a "buddy or partner system." The second night's program is announced and they are invited to bring their friends.

Thus, each evening a new facet of the tobacco habit is discussed, and new insights are given the individual on how to cope with his problem of addiction.

For The Discouraged Participant

A word is in order for the individual who doesn't quite make it—perhaps he slips up, he sneaks one now and then, or perhaps he cannot see himself stopping all at once. In any case, we encourage him to keep coming; we will help him. This habit is not easy for some to break. We try to do nothing that would discourage or cause them to think they are helpless. We explain from the outset that some may find it difficult to follow all the suggestions that are given; on the other hand, the closer they follow the rules, the faster the withdrawal symptoms are over, and the sooner they can really begin to live.

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* "One In 20,000" film produced by American Temperance Association, 6840 Eastern Avenue, N. W., Washington, D. C. This film is now several years old, but is still very effective. It is our policy to give a brief explanation of the surgical scenes before the film is shown. This allays the fears of anyone who might be a bit sensitive, or have a tendency to faint at the sight of blood. We feel that such an announcement is important in showing this film.

Follow-Up Meetings

We have a follow-up meeting the next week after the Five-Day Therapy Sessions are completed and lay plans for future weekly and/or monthly meetings. It is most essential that a strong follow-up program be conducted. This will be treated in more detail in later reports.

Report Of Calgary, Alberta, Canada Program

Because the results in Alberta, Canada during the Five-Day Program are similar to those in the States, we are here giving the early results of that particular session.

On September 8 through 12, 1963, the Five-Day Program to Stop Smoking was conducted in the Palliser Hotel ballroom in Calgary. Those attending the course were all adults and were from the same strata socially as those of the groups in the States—(middle to upper class). Of the 192 who signed up to take the course, 144 finished by attending the majority of sessions (three out of five sessions). Of the 144, there were 74 men and 70 women, the average age being 37 years. Results are tabulated according to Ejrup's[7c] classifications:

1. The number who stopped smoking was 104 or 72.2 per cent of those who actually attended the majority of the sessions.
2. The number who reduced their smoking to 25 per cent or less was 23 or 16 per cent.
3. Those still smoking at the end of five days (26-50 per cent of previous consumption) was 10 or 6.9 per cent.
4. Smoking (51-100 per cent of previous consumption) was 7 or 4.9 per cent.

Those in categories (1) and (2) are classed as good results; that is 72.2 per cent stopped altogether and 16 per cent reduced their former consumption to 25 per cent or less, or a total of 88.2 per cent. Those in categories (3) and (4), 11.8 per cent, are classed as poor results.

We have discovered that 33.9 per cent of those taking the course are still maintaining their non-smoking status at the end of a three-month period. Of those who returned to smoking, many felt that they would benefit by another Five-Day session or by regular follow-up meetings.

We would like to emphasize that these figures and percentages are not fixed. This is a preliminary report. We are trying to get an accurate accounting of the 48 individuals that dropped out, or failed to make an appearance. We want to know *why*. This answer will help not only us, but others[6] who have noted a reluctance to "go through with their good intentions."

Likewise we know that 33.9 per cent remaining on a non-smoking basis at the end of three months is far from being a fixed percentage. This may be radically influenced by who comes; why they came, and whether they *want* to quit or not; who presents the Five-Day Program; what type of follow-up is conducted. We have reason to believe that the number of individuals that remain non-smokers is dependent on a careful follow-up such as weekly or monthly meetings. Our impression is that we will get close to 50 per cent if a careful follow-up program is conducted.

Another factor pointed out by Hammond and re-emphasized by Garfinkle,[5a] one of his co-workers, is the fact that there is a certain percentage of individuals who have stopped smoking regardless of any therapy. They did it on their own, having once made up their minds to break the habit. What per cent of these slipped into our good results, we are unable to state.

We do know that no individual needs despair of getting over the habit if he carefully follows out the instruction given.

Our figures of 70-80 per cent stopping their tobacco by the end of the Five-Day session is our most firmly established figure. Some of the teams we have trained are getting 80 per cent and beyond consistently in their program.

Final Results And Conclusions

We are in the process of determining how long those who have taken just the Five-Day course maintain their non-smoking status. We are also accumulating data on some of the most pertinent withdrawal symptoms and also the beneficial effects from giving up smoking. We are certain by spot checks on our earliest programs that a follow-up program is very essential. The individual who has recently given up smoking in a group therapy setting needs the bolstering of association and sharing his experience with others. This cannot be too strongly emphasized. Such a follow-up program has now been set up on the basis of monthly meetings.

We are certain that large scale group gatherings can help many to overcome the habit of smoking. We have conducted thirty-three (33) such programs throughout the United States, most of them being in small New England towns. Teams have been trained which are continuing the program in the United States and Canada. The size of the groups has varied from 12 to 400 individuals. Although most of these have been adults, we have held classes in high schools and junior high schools for students who desire to stop smoking.

This report is primarily concerned with observations on what is included in the Five-Day Plan to Stop Smoking, and how these group therapy sessions are conducted. It is apparent that it is not only feasible, but workable with large group gatherings (400 or more individuals). We are able to state that in over 1,500 individuals who carried out the program, approximately 75-80 per cent have, within five days, lost their craving to smoke, or the craving is so much less that they feel they can manage the problem. Fifty per cent usually notice some benefits by the end of the third day. Taste and smell often return by then. Twenty to twenty-five per cent will need to continue another five days. Of this latter group, a small per cent may need to be in a clinic where they can have constant medical supervision with added medication.

It is time that the medical profession carry forward an active program to assist large numbers who wish to "kick the habit" to stop smoking. Facts alone will not do this; although they are vital, a more comprehensive attack is needed with many.

A large scale public health educational program is called for, to alert, convict and help the tobacco addict to overcome his habit.

Summary

1. A preliminary report of the methods used in a Five-Day Program to help people stop smoking has been presented.

2. An all-out approach is made in all phases of living—physical, mental, spiritual, social and economic. A physician-clergyman team conducts the course.

3. The program consists of five one and one-half to two hour sessions of group therapy, using films, models, lectures, class discussion, and a "buddy system."

4. Approximately 50 per cent of individuals on the Five-Day Program will find the craving and withdrawal symptoms less by the end of the third day. By the end of the fifth day, 70-80 per cent will find the craving gone or so much less that they feel they can manage the problem. By this time most of the withdrawal symptoms will be over. The sessions held in Calgary, Alberta, Canada are reported.

5. A program for helping large groups of individuals who wish to stop smoking is feasible. Some such plan will be needed to assist an ever growing number of tobacco addicts who wish to stop smoking.

6. The medical profession should arise as one man and in every way possible, both by precept and example, urge that tobacco has no place in a sound physical fitness program. They should lend their influence individually and collectively on the side of preventing tobacco deaths, thus safe-guarding the public health and our richest heritage on earth, our youth.

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Some Historical Aspects Of Esophageal Surgery

James B. D. Mark, M.D.

Introduction

■ The history of esophageal surgery is the story of men — many men — who have made contributions both great and small to this field. A number of these men were not surgeons, since the development of thoracic surgery of any kind were severely limited prior to the knowledge of physiology of the open chest and the development of important ancillary aids for thoracic surgery. For these reasons, surgery of the esophagus, along with surgery of the heart and lungs, has been almost exclusively surgery of the 20th century. One does not have to reach far in to the past to find the men who have made significant strides in this field. They are our teachers or our teachers' teachers. In some cases, they are our co-workers, and may even in the future be our students, since the field of esophageal surgery remains an open book with many pages yet to be completed.

In the discussion to follow, no attempt is made to acknowledge every contribution or every contributor to this field. The important problems of endoscopy, esophageal diverticulum, achalasia and esophagitis are not discussed or are merely mentioned briefly. The purpose of this report is to focus specifically on only a few major problems in esophageal surgery and to review briefly the events which have led us to our present state of knowledge about them.

In the works of the classical medieval period and renaissance, little or no mention is made of surgery of the thoracic esophagus. As late as the mid-19th century, most of the contributions in the field of esophageal surgery were concerned with the cervical esophagus—the drainage of abscesses, the management of wounds and foreign bodies and the treatment of cervical esophageal diverticula. There seemed to be a great fascination in the development of better probangs for retrieving foreign bodies, and dilators for the management of strictures. By the latter portion of the 19th century, carcinoma of the esophagus began to be recognized clinically as an entity separate from benign stricture, and Billroth in 1871 first spoke of specific treatment for this lesion.[5] On May 2nd, 1877, the first esophageal resection in humans was carried out by Czerney, a former assistant of Billroth, who was then Professor of Surgery in Heidelberg. This was a resection of the cervical esophagus for carcinoma and the patient died in about a year of recurrent disease. Von Mikulicz stated in 1886 that carcinoma of the esophagus should be curable since there were only local metastases in 25 of 42 patients that he had examined at autopsy. Ten years later he attempted resection of the distal esophagus and cardia of the stomach for carcinoma by the abdominal approach but the patient died of peritonitis. It was at about this time (1895) that Wilhelm Röntgen[23] first reported the use of x-rays, which proved to be a tremendous diagnostic aid in esophageal disease.

By the end of the 19th century, narcosis, asepsis and antisepsis were accepted clinical concepts making possible the development of abdominal surgery. Still the thorax was shunned. There was almost a superstitious fear of intrathoracic surgery because of the great problem of open pneumothorax. It remained for Ferdinand Sauerbruch, through the stimulus of his chief or geheimrat, Johan Von Mikulicz, to make the first real sortie into the thorax by his development of the negative pressure chamber. Sauerbruch first tried a tight-fitting mask for thoracic surgery but gave that up for the pressure chamber. As Sauerbruch himself tells the story in his autobiography, he gave much thought to the problems of operating within the thoracic cavity. He did numerous experiments in the chamber before demonstrating it to Von Mikulicz. These experiments consisted of opening and closing the chest in experimental animals, a great feat in itself.[26]

He then told Von Mikulicz of his work. The geheimrat was skeptical, but finally consented to watch a demonstration. The experiment began, the pressure was adjusted and the rabbit's chest was opened. At this point, the chamber sprang a leak and the animal died on the spot. Sauerbruch improved his pressure chamber and was able to get Von Mikulicz to observe another experiment, this one successful. He reported his first 78 successful experimental operations in the chamber at the Berlin Surgical Congress in 1904. Sauerbruch's paper was entitled "On the Physiological and Physical Principles in Intrathoracic Operation in My Pneumatic Operation Chamber," and included

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a demonstration before the assembled throng. Both the paper and the demonstration met with immediate approval and thoracic surgery on the continent was on its way.

The first patient operated on in the pressure chamber was a woman with carcinoma of the esophagus. She died during the operation. The chamber had not functioned properly. The second patient was a woman with a mediastinal tumor. This time everything went well. Von Mikulicz was the surgeon in both of these cases. Sauerbruch operated the controls of the chamber.

In 1908, Sauerbruch was invited to the United States by Willy Meyer to demonstrate the chamber. He operated on animals at the Rockefeller Institute with the permission of the director, Dr. Simon Flexner. Willy Meyer then constructed his own chamber with the help of his brother, an engineer, and early in 1909, this chamber was moved to the old German Hospital, now Lennox Hill Hospital in New York, where it was used for thoracic surgery.[17] In that same year, Meltzer and Auer[16] at the Rockefeller Institute developed the technic of peroral endotracheal intubation for administering anesthesia. This was a much simpler and less cumbersome technic to insure satisfactory pulmonary ventilation during open thoracotomy, and because of its popularity, the pressure chamber was not widely used. No other chamber was ever built in the United States. Because of lack of space, the pressure chamber at the German Hospital was dismantled in 1923.

Carcinoma Of The Esophagus

In 1913, Wolfgang Denk, later Chief of Surgery at the Billroth Clinic in Vienna, described his operation for total esophagectomy. On March 14th of the same year the first major advance in surgery of the esophagus in this country took place. Franz Torek, also at the German Hospital, performed a total thoracic esophagectomy on a 67-year-old lady under general endotracheal anesthesia. The anesthetic was administered by Dr. Carl Eggers, an outstanding thoracic surgeon, a founder and first Chairman of the Board of Thoracic Surgery, and a President of the American Association for Thoracic Surgery.

Torek had previously performed a gastrostomy on his patient for feeding. A thoracotomy was done through the 7th intercostal space, cutting four ribs posteriorly to gain better exposure. Torek spoke of three major problems which he expected to encounter and solve during his operation in order to insure its success. First was the problem of inaccessibility of the esophagus behind the aortic arch. Secondly, Torek thought that division of the vagi above the level of the cardiac branches would lead to instant death. He dissected these nerves very gently and preserved them. Thirdly, he sought to avoid problems with blowout of the closure of the upper esophageal stump by doing a cervical esophagostomy. During the course of the operation, he found the tumor to be adherent to the left main bronchus and the latter structure was injured and repaired during the dissection. A hot coffee enema with whiskey and Strychnin was given at the end of the operation. Postoperatively, the patient did very nicely in spite of the fact that no chest drainage was used. The lesion proved to be an epidermoid carcinoma and she lived twelve years following her operation, finally succumbing to pneumonia. Esophageal reconstruction was never performed in this patient although an antethoracic tube had been proposed.

Torek performed this operation on March 14th, 1913. A report of this case was read before four surgical societies in New York between March 24th and April 7th of that year and it was reported several months later under the title "The First Successful Case of Resection of the Thoracic Portion of the Oesophagus for Carcinoma."[27] Dr. Torek never performed another transthoracic esophagectomy. In fact, of the next 25 such cases done at the German Hospital, only one survived the postoperative course.[28] In spite of this rather dismal turn of events, a new day in esophageal surgery was dawning.

Ohsawa[20] in Japan, in 1934, and Adams and Phemister[2] in this country in 1938, reported successful resection of carcinoma of the lower esophagus with primary esophagogastric anastomosis. Adams and his co-workers[1] studied experimental esophagogastric anastomosis systemically, as had Dr. B. Nolan Carter,[6] and Adams emphasized that tension at the anastomotic area must be avoided. Ohsawa had thought that the anastomotic problems were due to division of the left gastric artery in mobilizing the stomach and he, at first, assiduously avoided sacrificing this vessel although Kirschner almost 15 years earlier had demonstrated that the left gastric vessels could be divided with safety.[10] Adams and his co-workers confirmed by animal experimentation that the stomach maintained excellent blood supply from the gastroepiploic vessels alone, and that this organ could be mobilized into the chest without difficulty. Their first case was a 53-year-old woman with an epidermoid carcinoma of the distal esophagus. She weighed 37.5 kg. at the time of her operation, and lived over a year thereafter before succumbing to recurrent tumor. Garlock,[7] in 1944, did the first resection of a mid-esophageal carcinoma with supra-aortic esophagogastrostomy through the left chest. Nakayama, Professor of Surgery at Chiba University in Japan, later championed the combined right thoracoabdominal approach to mid-esophageal carcinoma in a report of 400 cases of carcinoma of the esophagus in 1954.[18]

This is about where we stand now with esophageal carcinoma. The technical feats of resection and reconstruction can be accomplished, albeit with a mortality rate higher than desirable, but cures are still few and far between. Possibly preoperative super-voltage x-ray will help. More than improvements in surgical technic, however, will be necessary to conquer this difficult disease.

Congenital Tracheoesophageal Fistula

Many indirect approaches for surgery of congenital tracheoesophageal fistula were used in the early part of the 20th century, although Richter, in 1913, had advocated a direct attack on the fistula.[21] Unfortunately, he was ahead of his time. Leven, in 1941, was the first to successfully approach the fistula directly, divide it and then do a cervical esophagostomy and gastrostomy, with antethoracic reconstruction at a later stage.[12]

In 1943, Haight[8] reported the first successful one-stage primary reconstruction in a case of tracheoesophageal fistula which he had carried out in 1941. Dr. Haight's first successful case was 13 days old at the time of the operation, having been transported by ambulance from some distance away with several stops for fluid administration. He used the left extrapleural approach and the case was complicated by edema due to improper fluid administration, and a leak at the anastomosis. On the 10th postoperative day, a feeding gastrostomy was done. At this time, a catheter could be passed through the mouth and out the chest wound. By the 20th postoperative day, the fistula had closed, and two months following operation, the chest wound had healed. This was the ninth patient with congenital tracheoesophageal fistula on whom Haight had operated by this technic. The others had been unsuccessful. Shaw and Samson had both tried this approach previously without success. One of Shaw's patients died from a transfusion reaction. In 1940, Lanman[11] reported 32 cases of tracheoesophageal fistula who had been operated on at the Boston Children's Hospital over the preceding 11 years using the direct approach finally used with success by Haight. All of these patients died, several from excess administration of intravenous saline in the early postoperative period. In spite of this concerted effort by many surgeons, Haight's was the first successful case and it is his name that we associate with the surgical treatment of congenital tracheoesophageal fistula.

The Future

As we look to the future of esophageal surgery, there remains much to be done. A better understanding of the physiology of the esophagus is essential. Motility studies and cinéradiography have proven helpful. The pathophysiology of reflux esophagitis remains an incompletely understood area in spite of the excellent work of Allison in England, Ellis in this country and others. The cure rate in carcinoma of the esophagus remains abysmally low and the whole complex of etiology and treatment of this lesion needs much investigation.

From the technical standpoint, esophageal replacement remains a challenge. Beck,[3] in this country in 1905, conceived the use of a tube constructed from the greater curvature of the stomach to replace the esophagus and Jianu[9] in Hungary reported the clinical use of this procedure seven years later. In the interim, in 1907, Caesar Roux[24] reported the use of an antethoracic jejunal segment for esophageal bypass. Reinhoff[22] used the transthoracic route for jejunal bypass in 1946. Two groups of French workers[13,25] reported the use of intrathoracic right colon in 1951, and Mahoney and Sherman[14] popularized this procedure in this country by their report in 1954. All of these operations are cumbersome and time consuming. Some sort of plastic substitute for the esophagus should be practical. Berman[4] has tried since 1952 to replace the thoracic esophagus with a rigid plastic tube with limited success. Other types of plastic substitutes and aortic homografts have been used experimentally, but clinical success with this type of replacement still escapes us. The esophagus and its diseases remain a challenge.

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Application Of Physical Diagnostic Methods

The real study of heart disease began only after percussion had been applied in diagnosis and Laennec had shown the scope of auscultation. When that was done a period of active application of physical diagnostic methods began and the steady round of discoveries in the diagnosis and pathology of valvular disease may have diverted attention from the less objective signs of angina pectoris. At all events, interest in the coronary arteries waned and interpretations of angina as a nervous disease began to multiply, although the real study of diseases of the nervous system had hardly passed the stage it was in while Laennec was alive. —George Dock, M.D., "Historical Notes on Coronary Occlusion: From Heberden to Osler. Frank Billings Lecture." J.A.M.A. 113: 563, August 12, 1939.

THE PRESIDENT'S PAGE

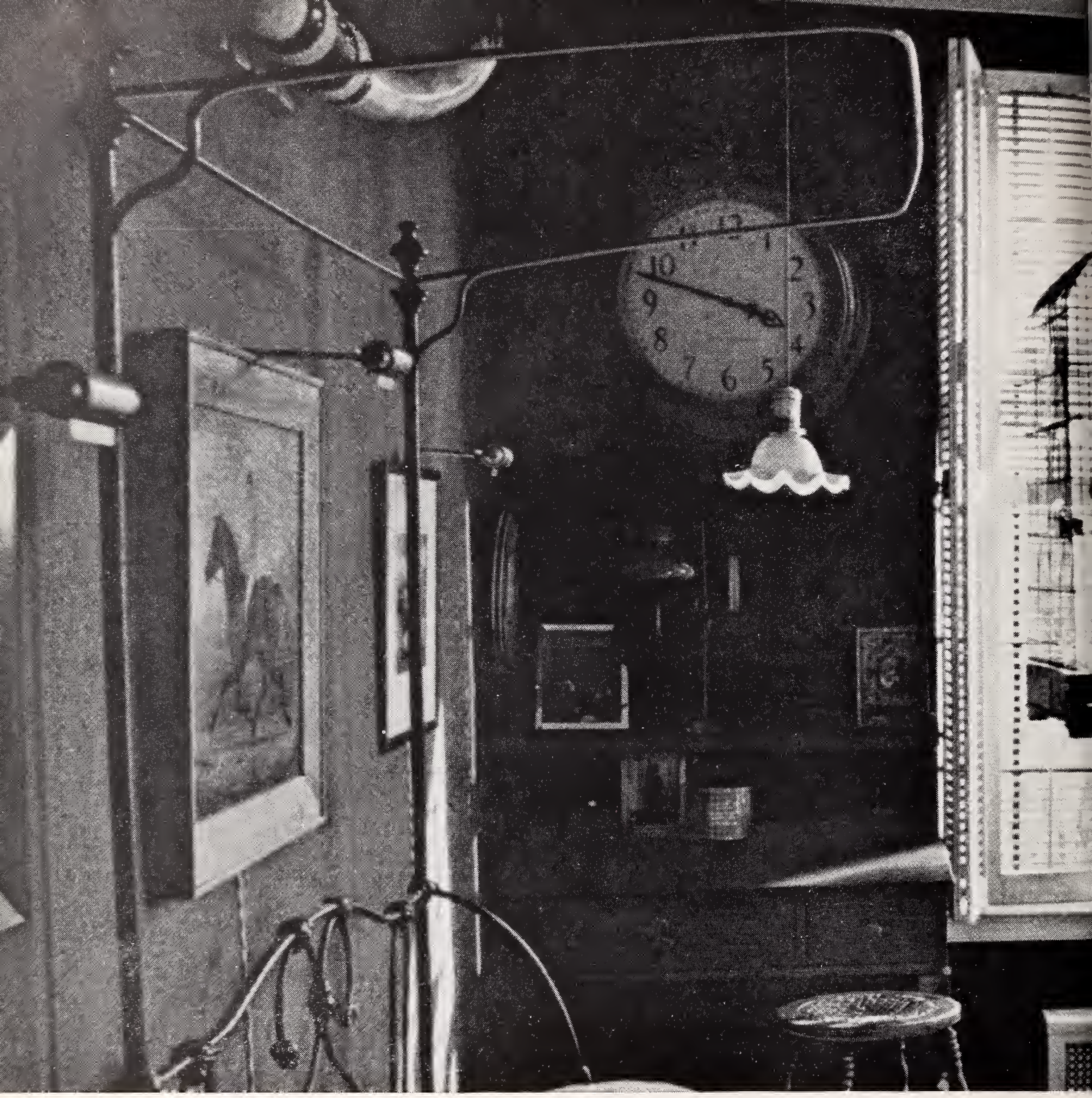
The tumult and the shouting of the past two months are over. The votes have all been cast and tallied. "The people" have spoken. Many and varied have been the pontifical pronouncements of those erudite pundits, the newspaper columnists and the radio and television commentators, as to what happened, how it happened, and why it happened. Many and varied also have been the conjectures of those same gentlemen as to just what "the people" said; just what mandate has been given to the Administration; and what legislative programs must and will be presented to Congress, and must and will be enacted. By and large these envision increasing centralization of government in Washington and the further expansion of federal control into and over the affairs of various segments of the private sector of American life.

What about the prospects in the never ending struggle to preserve in America the private practice of medicine, to keep off our necks the throttling bureaucratic control inherent in any and every governmental system providing medical care? It looks pretty grim, doesn't it? At the last session of Congress, the so-called Medicare Amendment to the Social Security measure in the Senate failed to become law only because the majority of the Conference Committee refused to accept it and the Administration preferred to scuttle the whole measure rather than to accept it without this provision. And the next Congress is no less, if not even more, committed to this program.

Here in Connecticut, we now have a Congressional delegation, all eight members of which can be counted upon to go straight down the line for whatever medical care program is introduced. This we know from their voting records or from the stand they have taken when questioned. Any attempts to present the point of view of the majority of practicing physicians in Connecticut with the hope of getting even a sympathetic reception, let alone any change of sentiment, will fall on deaf ears and be a futile waste of time and energy. However, medicine still has friends in Congress and our efforts will have to be channeled into encouragement and support of those who have been our allies in the past through whatever means are available.

The prospects certainly are not rosy; nor are they completely hopeless. All who believe in maintaining the freedom of the practice of medicine will have to unite and work for it more than ever before.

Ralph L. Gilman, m.d., *President*



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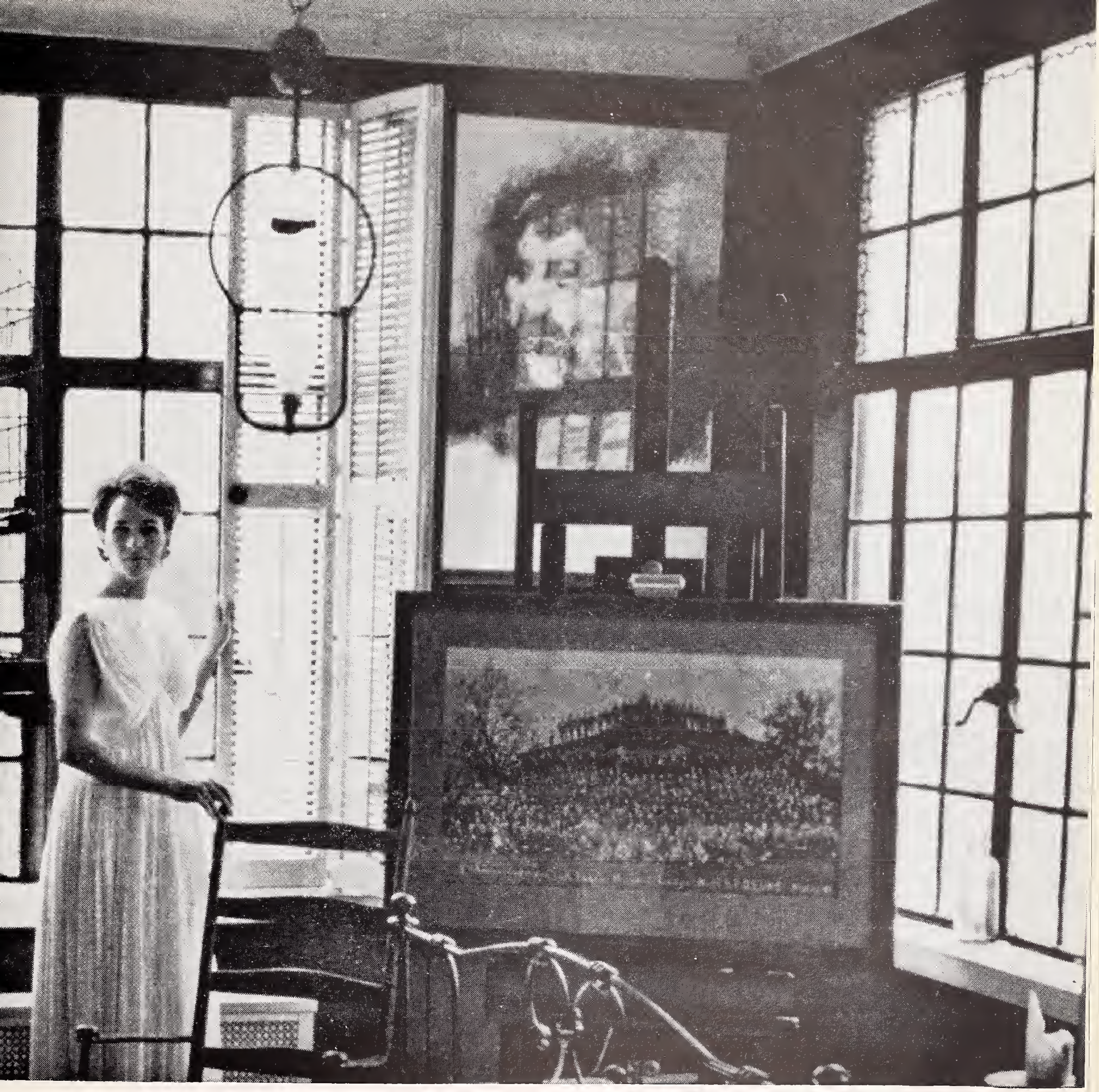

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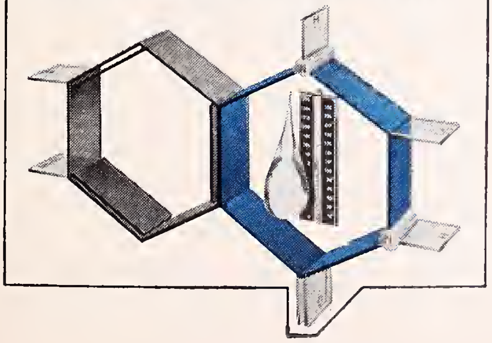

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8370-4

An Acute Abdomen Masked By Labor

Clarence D. Davis, M.D.

■ The patient was a 35-year-old Para III, Gravida IV, who was admitted in her thirty-sixth week of pregnancy in active labor, with the fetus presenting by frank breech, the membranes bulging and the cervix fully dilated.

Previous Obstetrical History

There had been three full term spontaneous deliveries without event.

Prenatal Course

The information available on admission was that of uneventful pregnancy. It was not until the third postpartum day that information to the contrary was revealed. This was that the patient had experienced the onset of "tightness and pressure" in her abdomen two days prior to delivery and that the evening before her admission, the patient had been seen in the emergency room complaining of severe abdominal pain and rectal pressure. She was considered to have been in false labor and sent home.

Hospital Admission

Shortly after admission, under gas, oxygen and ether anesthesia, the patient was delivered of a healthy child by podallic extraction of a frank breech without difficulty.

The postpartum course was considered to have been uneventful until the following morning when the patient was observed to be most apprehensive, with facial cyanosis and dyspnea. There was also noted severe abdominal distention with absence of bowel sounds. Examination of the heart and lungs did not suggest primary cardiac or pulmonary distress. The temperature and pulse were normal and blood pressure was recorded as 180/100. Prostigmine was given for the abdominal distention and the patient was placed on digitalis. The impression at this time was that the patient possibly had a coronary occlusion. The patient's condition became progressively worse and on the third postpartum day, for the first time, the temperature and pulse started to rise. A surgical consultation was requested.

A flat film of the abdomen showed evidence of intestinal obstruction. X-ray of the chest was negative as was an electrocardiogram and serum amylase. The hemoglobin was 96 per cent, hematocrit 48 per cent, white blood count 24,800, with 90 per cent polys. The blood sugar was 158 mg. per cent. The surgical consultant noted extreme distention of the abdomen with tympany, marked tenderness in both lower quadrants and hypoactive bowel sounds. Intravenous penicillin was given, and an hour later, an abdominal exploration was performed under pentothal and endotracheal cyclopropane. On opening the abdomen, a considerable amount of gas was released and a large quantity of grayish-yellow, foul-smelling exudate was present. Exploration revealed a subhepatic abscess on the left which was already walled off, involving the transverse colon. The bowel distal to this mass was collapsed, and the proximal bowel up to the ileocecal valve was dilated. There were also present multiple interlooped abscesses. No site of perforation was found, despite careful search. A transverse colostomy was done. At the onset of the operation the patient's blood pressure was 125/90, and at the end was 165/100. At this time, signs of heart failure appeared, and the patient was placed in an oxygen tent and continued on digitalis. A Levin tube was inserted and connected to a suction apparatus. The patient was also given intravenous furadantin. Culture of the abdominal exudate was positive for nonhemolytic streptococcus and gram-negative rods which were sensitive to furadantin, achromycin and chloromycetin.

The patient's condition improved progressively over the next few days with normal readings of blood pressure, pulse, respiration and temperature. Electrolytic studies were essentially normal. By the fourth postpartum day the patient was free of complaints, the Levin tube was removed, and clear fluids were taken by mouth. The patient was allowed out of bed with increasing ambulation over the next few days. However, from the fourth postoperative day on, there was a slight but progressive elevation of her pulse and temperature. Moderate distention persisted, and the bowel

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sounds remained hypoactive. On the seventh postoperative day, some purulent drainage was noted at the site of the colostomy. On the ninth postoperative day, the temperature spiked to 102, and the pulse rose to 104. The patient began to experience nausea with vomiting and diarrhea, and began to perspire profusely. On the tenth postoperative day, X-ray studies revealed elevation of the diaphragm with a suggestion of a small amount of fluid in the pleural cavities and a questionable soft tissue mass in the left mid abdomen. The clinical impression at this time was that of a postoperative general peritonitis with a subhepatic abscess. The patient was re-operated under pentothal, oxygen and ether anesthesia. The operation consisted of drainage of the left-sided subhepatic abscess, yielding approximately 500 cc. of pus, and evacuation of a small interlooped abscess. Several drains were placed. At the end of the operation, the patient became cyanotic and developed acute pulmonary edema. The patient was placed in an oxygen tent and given intravenous digitalis, hydrocortisone, chloromycetin and levophed. The patient became progressively comatose; temperature rose to 109 degrees and she expired three hours postoperatively. Autopsy was refused.

Comment

A diagnosis of peritonitis in prodromal labor is one of the most difficult diagnoses the obstetrician has to make. The information that was available was not sufficient to establish such a diagnosis at the time of her delivery. However, the information concerning the abdominal discomfort which the patient had experienced for two days prior to delivery, and of her emergency room visit, should have been available at the time of her admission. Had this been known and closer attention paid to the patient during the hours immediately following her delivery, less delay in the recognition of her peritonitis would certainly have occurred. Regardless of this, the observation on the first postpartum day of cyanosis, dyspnea and extreme abdominal distention should have led to further investigation and more prompt surgical consultation. Empiric digitalization without evidence of cardiac decompensation is to be questioned. The progressive abdominal distention was ignored until the third postoperative day; certainly this finding should have been treated as being most significant, and the possibility of an acute abdomen should have occurred to the observers. During the next two days, there was gross negligence, for it was not until the patient started to deteriorate that the proper diagnosis was entertained. Consultation was delayed and at least a full 48 hours were lost.

Because of the operative findings of a moderately well walled-off abscess, interloop abscesses, and the degree of involvement of the bowel, leading to the obstruction, the patient must have had her peritonitis for longer than 48 hours.

This patient was operated on as an emergency, with a hematocrit of 48 per cent and a hemoglobin of 96 per cent, without adequate attention paid to prior hydration. One wonders if the patient was not severely dehydrated at the time of operation. This might have been the reason for her deterioration into heart failure postoperatively. It probably would have been much better to take a few hours to get the patient in better shape for the operation. During the first operation, a Miller-Abbott tube should have been passed and fed through the duodenum to aid in decompression.

The judgment of the surgical consultant in not draining the subhepatic abscess at the initial operation might also be questioned. The choice of antibiotics might also have contributed to her demise, in that adequate parenteral doses of a broad spectrum antibiotic effective against gram-negative organisms were not employed. The patient's course between the first and second operations was one of initial improvement and then slowly but progressively running into difficulties as noted by the rise in temperature and pulse from the fourth postoperative day on. Again, when the situation was in the extreme, then and only then was anything done. The final surgery was done in desperation and futility. In the absence of a post mortem examination, the exact cause of the patient's abdominal catastrophe remains obscure.

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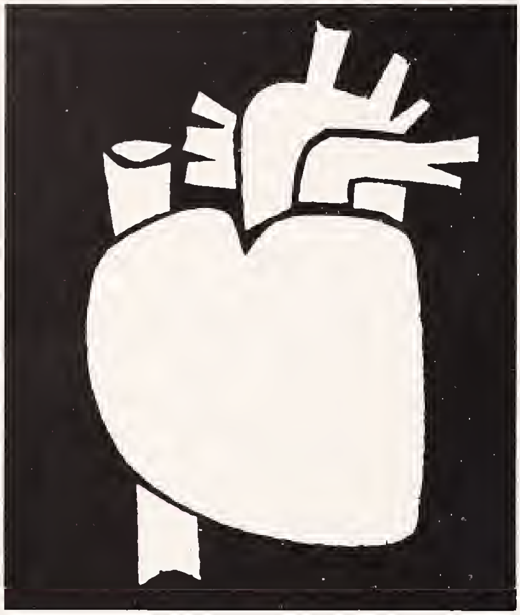

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Indications: 'Miltrate' is useful for prophylaxis of pain in angina pectoris and coronary insufficiency, especially where anxiety is a factor. **Contraindications:** Like all nitrates, pentaerythritol tetranitrate should be avoided or prescribed cautiously for patients with glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use. **Precautions:** *Meprobamate* — Patients engaged in activities requiring alertness should be warned of drowsiness. Meprobamate may increase the effects of excessive alcohol, and the possibility of dependence should be considered, particularly in patients with a history of drug or alcohol addiction. Sudden withdrawal may result in reactions, rarely epileptiform seizures. Grand mal attacks may be precipitated in persons susceptible to both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies. **Side effects:** *Pentaerythritol tetranitrate* — The most common side effects are transient headache, nausea, and rash. Weakness, palpitation, flushing, gastrointestinal distress, and lightheadedness have been reported on a few occasions. *Meprobamate* — May cause drowsiness and, rarely, ataxia, usually controlled by decreasing the dosage. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses of the drug. Mild reactions include urticarial or maculopapular rash. Serious reactions, rarely encountered, include dermatological effects, acute nonthrombocytopenic purpura, chills, fever, fainting spells, angioneurotic edema, bronchial spasm, hypotensive crisis, anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic, and the drug not be reinstituted. **Dosage:** Usual dosage is one or two tablets before meals and at bedtime. Individualization of dosage is required for maximum therapeutic effect. Doses above twelve tablets daily are not recommended. **Supplied:** White tablets, each containing meprobamate 200 mg. and pentaerythritol tetranitrate 10 mg. *Before prescribing, consult package circular.*

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FROM THE GENERAL MANAGER'S OFFICE

William R. Richards, m.d., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865-0587

James G. Burch
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, October 28, 1964

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gilman, Hess, Goldberg, Brandon, Davis, Weise, Sr., Gardner, Bradley, Grendon, Caplan, Phillips, Shepard, Ciccarelli, Seigle, Fabro, Egan, Abbott, W. Martin, Spitz, Hastings and Major. Also present were: Mrs. Lindquist, Mr. Burch and Dr. Richards. Absent were: Drs. Cullen, O'Connor, Pitock, Grant, Hughes, Ayres and Rogol.

II. Routine Business

Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of September 10, 1964, with the following amendment: Armanno W. Ciccarelli wished to be recorded as having voted nay on the Council's action not to endorse the "Five Year Plan for Chronic Illness of the Aging Activities, Connecticut."

Life Membership

It was VOTED to approve applications for Life Membership for the following Active Members:

Sara A. Bonnett, Ridgefield (FCMA)
William Cohen, New Haven (NHCMA)
William J. Dennehy, New Haven (NMCMA)
Chester E. Haberlin, Stratford (FCMA)
Andrew F. McGourty, Stamford (FCMA)
Albert J. Robinson, Madison (HCMA)

Resignation—Editorial Committee Of The Journal

It was VOTED to accept the resignation of William H. Resnik, Stamford, as a member of this Committee, and it was further VOTED to appoint John C. Leonard, Hartford, to complete Dr. Resnik's unexpired term on the Committee.

Resignation—Committee On County And Local Public Relations

It was VOTED to accept the resignation of Herbert Levine, Middletown, as a member of this Committee, and it was further VOTED to request the Chairman of the Committee to recommend a replacement for Dr. Levine to be appointed by the Council to complete his unexpired term.

Please Read ***Please Read*** ***Please Read***

IMPORTANT ANNOUNCEMENT

"Readership Survey" Questionnaire

From time to time speculation has been raised as to the reading habits of members of the Society with respect to Connecticut Medicine. The Editor and the Editorial Committee of the Journal have often expressed interest in conducting some type of survey which would furnish information about what features of the publication members like and what features they are less interested in or would prefer to have changed.

National advertisers, whose accounts help make the Journal possible, have also expressed a desire to know more about what the tastes of physicians are with respect to advertisements, and have asked us to supplement our statement of actual circulation with an estimate of the size of the Journal's "readership."

At the Council meeting of November 19, it was voted to conduct a direct mailing to all members of the Society, such mailing to consist of a questionnaire and a covering letter of explanation. The questionnaire will be brief and to the point, will call for a minimum of effort to complete, and will have a self-sealing feature to simplify returning it to the General Manager's office.

This mailing will be conducted during the month of January, 1965. The percentage of returns as well as the answers to the questions may prove to be of great importance to the future of Connecticut Medicine, and each member is therefore urged to be on the lookout for the questionnaire and to complete and return it promptly.

Appointments—Ad Hoc Committee On Resolution No. 2

It was VOTED to appoint J. Alfred Fabro, Torrington, and Nathaniel Selleck, Danbury, to membership on this Committee.

Resignation—Committee On Accident Prevention

It was VOTED to accept, with regret, the resignation of Malcolm S. Beinfield, Westport, as Chairman of this Committee, and it was further VOTED to appoint Abe S. Brown, Waterbury, a member of the Committee, to serve as Chairman for the remainder of the year 1964-65.

Report—Delegate To The Vermont State Medical Society

It was VOTED to receive as information the report of a Delegate to the Vermont Society, Charles T. Schechtman, New Britain, on his attendance at the annual meeting of that Society.

Report—Representative To AMA National Voluntary Health Conference

It was VOTED to accept the report of Henry Caplan, Meriden, on his attendance at this Conference as a representative of the Society, and to submit his report to the Journal for publication.

Report—Representative To AMA 4th National Congress On Health Insurance And Prepayment Plans

It was VOTED to accept the report of E. Tremain Bradley, Norwalk, on his attendance at this Congress as a representative of the Society, and to request Dr. Bradley to submit a summarized version of his report for publication in the Journal; also to furnish copies of the report to members of the Ad Hoc Committee on Resolution No. 2 and of the Committee on Third Party Payments.

Report—Representative To AMA 24th Congress On Occupational Health

It was VOTED to accept the report of J. Wister Meigs, New Haven, on his attendance at this Congress as a representative of the Society, and to submit his report to the Journal for publication; also to furnish copies of the report to members of the Committee on Occupational Health.

Appointment—Representative To AMA 1st National Conference On Areawide Health Facilities Planning, Miami Beach, Nov. 28-29, 1964

It was VOTED to request Max Caplan, Meriden, Alternate AMA Delegate, to represent the Society at this Conference and to file a report with the Council on the proceedings.

Appointment—Representatives To Connecticut Mental Retardation Planning Project

As requested by Mr. Eric Sandahl, Project Director, it was VOTED to direct the Chairman of the Council to appoint up to six representatives to serve with the "Task Force on Physicians and Mental Retardation" of the Project, such representatives to be divided between the fields of general practice, obstetrics and pediatrics on a geographical basis. The Chairman made these appointments as follows:

Ob.-Gyn.—James F. Loftus, Hartford; David F. Conway, New Haven
Pediatrics—Joseph J. Bellizzi, Hartford; Harrison S. Coombs, New Canaan
General Practice—D. Norman Markley, Hartford; John E. Donnelly, Bethany

Appointment—Representative To 15th National Conference On Disaster Medical Care, Chicago, Nov. 7-8, 1964

It was VOTED to confirm the Chairman's approval for John Shoukimas, Hartford, to attend this Conference as a representative of the Society, and to authorize reimbursement to Dr. Shoukimas for usual expenses incurred by his attendance.

Election Of Student Members

It was VOTED to elect 32 Connecticut residents attending schools of medicine to student membership in the Society. The names of the new Student Members will be published in the Journal.

Replacement—Council And Council Committees

Notice was received from the Middlesex County Medical Association that Richard F. Grant, Middletown, had resigned as Councilor from MCMA; that John R. Egan, Old Saybrook, Associate Councilor, had been appointed to replace Dr. Grant as Councilor for the remainder of his term; and that Joseph I. Epstein, Middletown, had been appointed to replace Dr. Egan as Associate Councilor from MCMA for the remainder of his term. It was VOTED to appoint Dr. Egan to replace Dr. Grant as a member of the following committees: (a) Committee on Loan Fund; (b) 1965 Budget Committee.

III. Old, New And Special Business

AMA Nutrition Educational Program

Max Caplan, Meriden, informed the Council that, at the request of AMA, his Advisory Committee on Nutrition and other groups are making plans to arrange seminars on nutrition at selected colleges in the state during the Spring of 1965. AMA will furnish the speakers for these seminars, and there will be no cost to the Society. It was VOTED to approve this project and authorize Dr. Caplan to proceed with arrangements.

Recommendations—Committee On Public Health

Four matters presented by the Committee on Public Health for approval by the Council were acted on as follows:

(a) It was VOTED to approve a statement for publication in the Journal and for release to the communications media that: "The Society recommends voluntary reporting by physicians of suspected cases of child abuse to the State Health Department.

(b) It was VOTED to confirm prior authorization by the Chairman that a member of the Committee attend a meeting of the American Public Health Association in New York, October 5-9, and that the member be reimbursed for usual expenses incurred by his attendance. It is expected that a report will be filed with the Council on the proceedings of the meeting.

(c) It was VOTED to approve a "Revision of the Public Health Code re Reportable Diseases" as recommended by the Committee.

(d) It was VOTED to endorse a statement on "School Health Education," prepared by Joseph J. Bellizzi, Chairman of the Advisory Committee on School Health, and to authorize its publication in the Journal

AMA Membership Dues

Anticipating that recommendations may be made to the Interim Meeting of the AMA House of Delegates concerning an increase in membership dues, it was VOTED to authorize the Society's AMA Delegates to use their best judgment.

Report—Ad Hoc Committee On Society's IRS Classification

Ralph L. Gilman, Chairman of the Ad Hoc Committee, reported on the study made of this matter by the Committee with the assistance of legal counsel. It has been determined that the Society now has a "business league" IRS Classification (501 C-6). With reference to a number of considerations relating to various operations of the Society, it is the opinion of legal counsel that there would be little if any advantage to having a "charitable and educational" classification (501 C-3) at this time. It was VOTED to accept the report of the Ad Hoc Committee and to approve its recommendation that the Society retain its 501 C-6 classification.

Communication—Group Insurers, Inc.

In response to two requests made by the Council, Group Insurers, Inc. of New Haven, administrators of the Society-sponsored "Overhead Expense Insurance Plan," made replies as follows:

(a) "(Concerning 'medical riders') we have undertaken an intensive program to remove medical riders. In the past two months, we have removed riders from six policies."

(b) "In connection with 'notification within one week' . . ., you have our assurance that every effort will be made to:

(1) Pay all claims within one week of receipt of proper claims forms, or

(2) Notify the claimant within one week if further medical information is necessary, or

(c) Notify the physician on the same day that we receive word from (the underwriter's) Claim Department that a claim will be denied. This, of course, might take a month or so, since we have no way of expediting physicians' and hospitals' reports to the Claims Department."

Progress Report—Committee On Hospitals

Leopold M. Trifari, Chairman of the Committee, filed a progress report on the subject of "Hospital Planning," with particular reference to discussions which have been held on this subject in joint conference with the Council on Professional Practices of the Connecticut Hospital Association. Expressing the opinion that "medical and paramedical opinion must be given appropriate weight with that of hospital administration if sound programs of this nature are to be evolved," the Committee made recommendations which it was VOTED to approve as follows:

(1) That the Council convey its concern in this matter to each of the component county medical associations, and urge each association located in an area in which a local or regional hospital planning group is currently operating to seek active participation in the planning activities of that group.

(2) That, at state level, the Council reiterate to the Board of Trustees of the Connecticut Hospital Association the Society's keen interest in all activities related to hospital planning, and reaffirm the Society's desire to be invited to provide representatives to participate during the developmental stages of all statewide programs concerned with that subject.

Inquiry Re CSMS Membership

J. Alfred Fabro, Associate Councilor from LCMA, inquired as to the existence of a contingency between CSMS and county medical association membership. Referring to the CSMS Bylaws in which it is stated that "Active Membership shall be *limited* to those members of component associations who are certified to the General Manager as entitled to exercise all rights of membership in their component associations, including the rights to vote and hold office," the Council advised Dr. Fabro that questions concerning contigent memberships should be resolved at county level.

Inquiry—Pharmaceutical Literature

It was VOTED to refer an inquiry made by J. Alfred Fabro, Associate Councilor from LCMA, to the Joint Conference Committee with the State Pharmaceutical Association for study and report. The inquiry was: ". . . should a drug company keep up the literature it offers physicians about its own drugs?" . . . "Should the Society suggest that drug companies always have up-to-date literature on their drugs?"

Inquiry—Formation Of A CSMS Judicial Council

It was VOTED to refer an inquiry on this subject made by J. Alfred Fabro, Associate Councilor from LCMA, to the Subcommittee to Study and Revise the Bylaws for evaluation and report. The inquiry was: "Should CSMS form a committee analagous to the AMA Judicial Council?" . . . "Its function would be to discuss ethical questions brought up by members of the Society. Questions could be practical—or even hypothetical (and) conclusions would have no weight unless so stated by the (CSMS) Council."

Request For Legislation—Section On Ophthalmology

It was VOTED to refer to the Committee on State Legislation, for implementation and pursuance, a Council-approved bill proposed by the CSMS Section on Ophthalmology which would amend the statutes in such a way as to authorize ophthalmologists (M.D.'s) to fit and dispense contact lenses and other optical aids to their own patients, whom they have examined and for whom they have prescribed, and would further authorize ophthalmologists to hire opticians or optometrists to assist in such fitting and dispensing in the doctors' offices and under their supervision.

Further Discussion—"Five Year Plan For Chronic Illness And Health Of The Aging Activities"

Pursuant to the Council's September 10th action not to endorse the draft report submitted by the Health Department on this "Five Year Plan" for Connecticut, Drs. Franklin M. Foote, Harold S. Barnett, Ira V. Hiscock, Norton G. Chaucer, and Ronald S. Beckett joined the Council to elucidate the programs and objectives embodied in the plan. In addition, correspondence was read which had been received from the CSMS Committee on Aging, the Board of Directors of the Hartford County Association, and Dr. Kurt Pelz, Wallingford. Dr. Foote and others presented and amplified a revised "summary and conclusions" section of the Five Year Plan report, and replied to a variety of questions posed by members of the Council. The essence of the exchange of ideas may be expressed as follows: Dr. Gilman stated that his concern (and that of the Council) was that the Plan seemed to call for the setting up of a central government agency in Connecticut which, in "coordinating" all agencies and facilities concerned with the subjects of the report, would or might assume control over voluntary as well as state agencies and even over the efforts of private practitioners of medicine in these fields. Dr. Foote assured Dr. Gilman and the Council that this certainly was not the intent of the Plan and that planning in this area would not result in "control" over voluntary groups or individuals. He felt that further revisions might help to clarify this and other points. Acting in a suggestion of Commissioner Foote, it was VOTED to direct the Chairman to augment the Society's representation on the planning group by appointing several members of the Council to serve with the three previously appointed physicians (Drs. Pelz, Chaucer, and Beckett) as advisors to the planning project. This Committee of advisors is authorized to assist in any way possible, especially with reference to drafting of the final report on the "Five Year Plan."

Dr. S. J. Martin, Chairman, subsequently appointed the augmented Committee as follows:

Ralph L. Gilman, Storrs, Chairman—(Council)
Ellwood C. Weise, Sr., Bridgeport—(Council)
Stewart P. Seigle, Hartford)—(Council
Ronald S. Beckett, Hartford—(Cancer Coordinating Committee)
Kurt Pelz, Wallingford—(Committee on Aging)
Norton G. Chaucer, Hartford—(Committee on Public Health)

It is anticipated that when the final report on the Five Year Plan has been drafted, it will again be submitted to the Council for possible endorsement on behalf of the Society.

COMPAC

Pursuant to the report of Dr. Gilman's Committee on IRS classification, Kenneth F. Brandon, Hartford, informed the Chairman that he intended to submit a second request for the Society to make a corporate gift to COMPAC for political education purposes, such request to be considered at the next meeting of the Council.

CMS Advertising In Journal, Etc.

Representatives of the New Haven County Association reported that the Board of Governors of NHCMA voiced strong objection to the Council that CMS advertisements continue to appear in Connecticut Medicine, despite the severing of relations between the Society and CMS and the circumstances surrounding same. After considerable discussion, it was VOTED *not* to renew an advertising contract with CMS when the current contract expires (January, 1965).

It was further VOTED *not* to accept CMS as an exhibitor at the 1965 Annual Meeting and Scientific Session.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on October 28, 1964. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

NEW MEMBERS

New Haven County

Frederick R. Amore, New Haven
Carl M. Cassin, New Haven
Gerald N. Cimmino, Derby
Ransey Cole, New Haven
Henry J. Cutler, Waterbury
Theodore Czuj, Rocky Hill
Louis DellaValle, New Haven
Peter Demir, New Haven
Philip R. Fazzone, New Haven
William H. Fisher, Jr., Waterbury
Harvey L. Fritz, Meriden
Willard S. Gold, Meriden
Johanna R. Haig, North Haven
Gilbert E. Holtzman, New Haven
Malcolm R. Ing, New Haven
Henry G. Jarecki, New Haven
James T. Keegan, Milford
Kisik Kim, New Haven
Bernard Kramer, Wallingford
Julius Landwirth, New Haven
Richard P. Lena, New Haven
Gilbert S. Melnick, New Haven
Patrick H. Mulhern, North Haven
Robert H. Ostberg, New Haven
David P. Reed, Waterbury
Nicola P. Romano, Rocky Hill
Robert S. Rosnagle, New Haven
Louis Schlessel, Hamden
Robert G. Selker, New Haven
Bernard S. Shapiro, Derby
Jerzy J. Sikorski, Derby
Mark W. Steele, Southbury
Michael L. Stein, Branford
John F. Summa, Waterbury
Allan L. Toole, New Haven
Robert L. Willenkin, New Haven
Barry M. Winters, Milford
Christopher M. Wiseman, Milford
Alvin Wolfson, Milford

New London County

Thomas J. Cook, Norwich
Paul R. Fleisher, New London
Frank G. Marx, New London
Alfred B. Vandersluis, New London
Yoshizo Nakano, Norwich

Middlesex County

Thomas P. Lambe, Middletown
Peter E. Spalding, Portland

Tolland County

Michael P. Atkins, Rockville
Barbara L. Fiedler, Rockville
James S. Harrop, Stafford Springs
Adele M. Perlman, Rockville

Windham County

Joseph E. Bouthillier, Plainfield
Arthur Diaz, Willimantic
Anne H. Dodd, Willimantic
Brian A. Dorman, Putnam
Maria N. Nepomuceno, Willimantic

PLACEMENT WANTED

General Surgeon — good experience in general surgery, urology, orthopedics and gynecology wishes to locate in rural area with available surgical facilities.

G.P. and General Surgeon wishes to locate in Southern Connecticut in either group or partnership practice.

General Surgeon—seeks either group or partnership practice in Southern Connecticut. Board eligible, 33 years of age, military obligation fulfilled.

Internist—Board eligible, University background, particular interest in chest diseases. Seeks either group or associate practice in Connecticut.

Obs.-Gyn.—seeks practice with group or clinic with possible academic affiliation, Board Diplomate, 37 years of age, presently on faculty of Department of Obstetrics and Gynecology, University of Louisville School of Medicine.

PLACEMENT OPPORTUNITIES

G.P.—One or two general practitioners wanted in town of Windsor Locks, Conn. Small town near Hartford with possible practicing rights at Hartford Hospital.

Opportunity for Board eligible or Board qualified Pediatrician, Orthopedist and Radiologist to associate with group of specialists in newly constructed building to be completed July, 1965. New Haven hospitals close by.

EENT PRACTICE – NEW YORK STATE: Physician deceased September 15, 1964. Executrix of estate agreeable to arranging terms for qualified specialist to continue practice, purchase office equipment, etc. Inquiries should be addressed to: Mrs. Theo B. Sheldon, 101 E. Henley Street, Olean, N.Y.

TUBERCULOSIS CONTROL PHYSICIAN needed by office of TB Control, Hospital Care and Rehabilitation of State of Connecticut. Will assist in carrying out public health education program; assist planning, organizing and supervising of case-finding activities. Will work with private physicians, lecture on problems of TB Control. Some clinic work. Salary ranges from $11,640-$15,080. Full benefit coverage. Reply directly to R. C. Edson, M.D., Office of TB Control, Hospital Care and Rehabilitation, 79 Elm Street, Hartford, Connecticut.

ANY PERSONS INTERESTED IN THE ABOVE ARE ASKED TO COMMUNICATE WITH THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN.

THE ARTHRITICS WHO COULD NOT TAKE STEROIDS

The bane of the steroids, new and old, has been tha certain undesirable metabolic effects — including sa and water retention, edema, overstimulation of th appetite, excessive weight gain, mood swings - seemed to be firmly linked to the primary ant inflammatory action. For arthritics already overweigh or with cardiovascular disease complicated by edema or those who were tense and anxious, steroid trea ment could aggravate their problems. But with th advent of ARISTOCORT® Triamcinolone, many o these arthritics became "steroid-treatable." The rea son: Not only did *this* steroid provide gratifying relie of inflammation and pain, but it did so *without* th penalty of overstimulation of the appetite, excessiv weight gain, salt and water retention, edema, an undesirable euphoria. Six years of widespread use ha confirmed these benefits for other arthritics as well a those formerly untreatable.

Side Effects: Since it may, under some circumstances, produce many of the unwanted effects common to all cortisone-like drugs, discrimination should always be exercised in administering ARISTOCORT® Triamcinolone. Any of the Cushingoid effects are possible, as are purpura, G.I. ulceration, increased intracranial pressure and subcapsular cataract. Corticosteroids generally may mask outward signs of bacterial or viral infections. Catabolic effects to watch for include muscle weakness and osteoporosis. Weight loss may occur early in treatment but is usually self-limiting. *Contraindications:* While the only absolute contraindications are tuberculosis, herpes simplex and chicken pox, there are some relative contraindications (peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, psychic disturbance, pregnancy, infection) to weigh against expected benefits.

A single daily dose may provide effective control, is convenient for the patient, and can be employed in both initial and maintenance therapy.

MAXIMUM STEROID BENEFIT—MINIMUM STEROID PENALTY

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Triamcinolone
scored tablets of 1 mg., 2 mg., 4 mg., 8 mg. or 16 mg.

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Synopsis Of Report

Fourth National Congress On Voluntary Health Insurance And Prepayment Under Auspices Of Committee On Insurance And Prepayment Plans Council On Medical Services Of The A.M.A.

Las Vegas, Nevada, October 2, 3, 1964

"Conservation of the Health Care Dollar" was discussed by panelists in two sessions and by audience participation in small groups during the intervening session, and by the Commissioner of Insurance of Nebraska. The panelists represented each of eight categories: the Consumer, Management, Labor, Hospitals, the Blue Plans, Independent Plans, Insurance, and Physicians.

It was generally agreed that the public expects to be kept well in addition to receiving care while sick. With the tremendous advancement in medicine, the percentage of national income expended on medical care has risen in the last thirty years from 3.9 per cent to 5.7 per cent. Of the health care dollar, hospital payments have risen from 14¢ to 30¢, while payments to physicians have fallen from 33¢ to 24¢. Although 75 per cent of the people have some health insurance, only 25 per cent of total medical bills are covered, and less than 10 per cent of doctors bills outside the hospital are covered. Ideally, all medical expenses should be covered by insurance. Yet, since processing small claims is uneconomical and raises premiums unduly, certain semi-predictable items should be budgeted, along with rent, food, and automobile repairs. Not only in voluntary insurance with private practice would this be true, but also in group plans and in any form of government medicine. Coverage by two policies, as when a husband and wife work for different organizations, was frowned upon by some though others pointed out that without unnecessary utilization (and this is rare) it should not affect the insurance system.

Employees need instruction about their insurance policies when filing claims, not just when buying the policy. In fact, "Education" is paramount: that good medical care is expensive, that insurance is to cover the unexpected, that the cost of insuring total care would be exorbitant, that claims should be spot checked by the "smell test" without reviewing all claims, that administrative costs of insurance should be kept low.

Health care is a big business and conservation of its finances means efficiency and not just diminution of cost. The decision as to whether new hospitals should be built or larger ones increased, and the design and architecture of additions and of new hospitals require the best judgment of planners, particularly doctors. Utilization committees which would act as combined coordinator, efficiency expert and expediter, were advocated—within the hospital, within the medical society, and between the two.

Commissioner Frank J. Barrett stated specifically that conservation of the health care dollar starts with the physician on whose authority the patients are admitted or are not admitted to the hospital, tests are performed, discharge from the hospital is ordered, etc. Doctors should deny unnecessary admissions. He advised insuring agents to cover services in nursing homes, doctors' offices, and elsewhere. He emphasized that buying insurance is different from buying a car, dress, or television because "non-use makes it a good buy." He stressed that health care is *not free!*

The Congress as a whole was indeed stimulating and thought-producing. The following constitutes the major constructive ideas extracted by your representative:

"No system can be all things to all people—at a reasonable price."

All parties must be educated. Of course the problem needs definition, and a survey was suggested. Formal facts for education would vary depending upon where or at whom it was directed.

The doctors, in whose hands lies the prime responsibility for the conservation of the health care dollar, must realize their responsibility in admitting patients only when medically necessary, discharging them at the earliest time permitted by medical indication, eliminating out-patient and in-hospital extra tests which could be avoided by the practice of good clinical medicine, substituting oral medication for injections when possible, teaching patients constantly about costs of medical care, helping to determine if new hospitals are really needed or whether existing facilities should be improved; establishing Utilization Committees to promote efficiency of practices in hospitals and in private practice, establishing Review Committees for the help and protection of the patients, doctors, and insurers.

The public should realize that health care is not free, that it is available and should be used but not wasted, that quality care should be recognized, that the government should not be relied upon to solve all problems.

Management should develop health programs oriented along public health lines, insist that company health examinations include better histories and physical examinations and only individually selected tests, help employees with their insurance when they need it more than when they are buying the policy.

Hospitals should be encouraged to develop modern methods of administration such as uniformity of accounting, improved billing systems, purchasing supplies in quantity and drugs by generic name, increased automation, utilization of facilities more hours per day and more days per week—even to getting outside professional advice or actually hiring contractors. The total sequestration of beds for obstetrical use should be avoided. The hospital should run on less "down time."

Labor which advocates—properly—treatment of the entire individual should be taught that total prepayment is uneconomical whether through government or insurance, that medical care is not free, that the quality of personal treatment under government control would undoubtedly be inferior to that received in private or even group practice.

The insurance industry must seek to improve the policies offered, to increase the coverage of total medical costs, to eliminate more exclusions from policies, to insure out-patient and nursing home services, to minimize over (duplicate) insurance, though before taking drastic action the public must be educated on this score.

There must be quality control of medicine. All interested parties should take a pioneering approach to bring good health care to all people.

While no magic solution evolved from this Congress, there was communication—and communication leads to understanding — and understanding leads to better joint planning and perhaps eventually to an effective conclusion.

E. Tremain Bradley, m.d.

Report On The A.M.A. National Voluntary Health Conference

The first national voluntary health conference was held in Chicago on September 17 and 18, 1964, under the sponsorship of the A.M.A. Council on Voluntary Health Agencies. The magnitude of this undertaking is illustrated by a directory which the A.M.A. published that lists sixty-two national voluntary health agencies. Indeed, there are more which are not listed; for example, the Community or United Funds.

The A.M.A. Council does not accredit any voluntary health agency. It expresses the American voluntary health movement as a unique phenomena which embodies three major freedoms—freedom of the individual, freedom of enterprise and freedom of association. National voluntary health agencies have now become an accepted part of our culture. They offer a wealth of opportunity for dedicated citizens to freely associate to promote good health in their community, state and country. They reflect the interest and concern of the American public with the improvement of health and the eradication of disease. They are effective channels through which individuals, doctors and laymen, can actively demonstrate an interest in community affairs.

A number of questions were critically discussed. Among them were the following: "What ethical consideration should be involved in soliciting public funds for health with respect to fund raising methods, advertising and reporting to the public?"; "How can we best attack the problem of over lapping and reduplication?"; "Are existing criteria helping to solve the problem of agencies which do not meet desirable standards?"; "Would state legislation help?"; "Is there a need for a set of national standards which would be used in accreditation?"; "Should all voluntary health organizations have programs including research, education and service?"; "Should there be a partnership between voluntary health agencies and government agencies in respect to research?", etc. etc.

The question of the desirability of state-wide or regional conferences with the active support of medical societies to encourage joint planning, perhaps utilizing common facilities, periodic evaluation and fiscal responsibility and public reporting was critically discussed. The question of accreditation was taken up. Who was to do the accrediting — the state? The A.M.A.? The National Health Council? Some other agency? Most delegates expressed the opinion that there be some form of accreditation and that the A.M.A. or the National Health Council be in charge. The opinion was far from unanimous.

It was impossible to attend all the conferences. I was particularly interested in the problem of overlapping and reduplication. There is no doubt that this exists. None of us want to be solicited almost every week and, at times, to give not because of the worthiness or effectiveness of the organization but because it is easier to part with a few dollars than to say no to a friend or neighbor. In the directory I mentioned previously, there are four national Epilepsy agencies each with its own offices, board of directors and fund raising program. There are listed three national Blindness and Sight organizations, three Cancer societies, four Maternal

Health agencies, two Deafness societies, numerous Neuromuscular and Physical and Mental Rehabilitation organizations, etc. The question rises as to why some of these organizations can not or will not amalgamate. Some of the delegates even believed overlapping was necessary and desirable since one organization might stress one aspect and another might stress an entirely different aspect of the same health problem.

There were group discussion summaries presented at the end of the conference which showed tremendous variations and differences of opinion in the best tradition of American Voluntarism. Dr. Blasingame spoke on The Future of American Medicine and there was also an address by Dr. Leonard Scheele, former surgeon-general on the Values and Virtues of Voluntarism. Both stressed that only in voluntarism could this country remain free.

Henry Caplan, m.d.

24th Congress On Occupational Health
And
Meeting Of Chairmen Of State Medical Association Committees On Occupational Health
Houston, Texas
September 26, 27, 28, 1964

As a representative of the Connecticut State Medical Society the undersigned attended these meetings. The majority of papers and presentations at the Congress came from specialists outside the field of occupational medicine. Thus, the symposium on "Cardiology in Industry" was presented by three professors of internal medicine and one professor of nutrition. The symposium on "Treatment of Burns" was presented by hospital based surgeons. The rehabilitation session was presented by specialists based in a large rehabilitation center.

These speakers were well qualified and their material was presented in an interesting way, however most of it was not closely related to occupational medicine. Furthermore, the sessions presented by specialists in occupational medicine were somewhat general in nature. Virtually no supporting data, for example case reports or epidemiological data were offered by any of the specialists in occupational medicine. This contrasted with several presentations by outside specialists and with that by an industrial hygienist.

The contrast between papers and speeches by specialists in occupational medicine and specialists in other branches of medicine should be a matter of grave concern to all of us in occupational medicine. We cannot remain "specialists" unless we produce new knowledge by practice and study of our specialty. Such new knowledge must be useful to our fellow specialists and must further identify the nature of our specialty to us and to physicians in other specialties. The 24th Congress on Occupational Health continued the unsatisfactory situation in which specialists in other areas tell occupational physicians how to practice occupational medicine.

In our Committee meetings this problem has been raised and it will be a matter of continuing consideration in the ensuing year.

The meeting of State Chairmen was of considerable interest. The entire day was devoted to discussion of a report of a special committee of the International Association of Industrial Accident Boards and Commissions on Workmen's Compensation Laws. Any full report is impracticable but one item regarding choice of physician is of interest in Connecticut. Of State Chairmen present, including several from so-called "free choice" states, only one was prepared to support without reservations the position that "the injured workman shall have free initial choice of the physician who treats him." It was emphasized that "free choice" is being urged most vigorously by spokesmen for special interest groups who wish to control the choice of physician for their own purposes. It was the concensus of the group that the AMA should support the principle of individual state responsibility for workmen's compensation legislation, keeping in mind the primary goal of the health of the injured worker.

Respectfully submitted,

J. Wister Meigs, m.d., *Chairman.*
Committee on Occupational Health.

The Physician Looks At School Health Education

Good Health is necessary to an individual, if he is to gain fully from his educational experiences and to have the best opportunity to stand up to life and reach his goals. There is, then, an obvious inter-relationship between health and education and, in fact, health has long been recognized as an expected outcome of education.

Since 1912, physicians and educators have worked cooperatively through the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association to encourage health education programs in schools. Much has been accomplished, but much remains to be accomplished, primarily due to the rapid changes occurring in the world today.

The price of progress is change and adjustment. Health education is not spared from these forces. Medical progress has expanded the concept of health from a disease oriented approach to one defining health as a state of physical, mental, and social well-being. The emphasis, therefore, is more on the "positive process of living" rather than on the "negative prevention of disease." Life is considered a developmental process with intrinsic capabilities, constantly influenced and guided by the individual's milieu.

Since education is a prime motivating force affecting behavior, it has the responsibility of assisting the individual to become aware of, to understand, and to develop more mature, intelligent, and responsible attitudes toward living. School health education programs, then, must be initiated, reviewed, evaluated, and replanned to meet the evolving current and future needs of the society in which he lives.

To attain these goals, the school health education program must be a well planned basic subject in the school curriculum. The content of such health courses should consist of the facts and principles of healthful living pertaining to individual, family and community health. Desirable areas for instruction have been listed as follows:

1. Accident prevention and first aid
2. Food and nutrition
3. Activity, sleep, rest and relaxation
4. Physical growth and development
5. Clothing, cleanliness and grooming
6. Mental and emotional health
7. Structure, function and care of the human body
8. Family life and health
9. Teeth and dental health
10. Prevention and care of sickness
11. Community health
12. Consumer education
13. Alcohol, tobacco and drugs
14. Health careers

In the effective teaching of these facts and principles, the student's developmental characteristics, interests, cultural backgrounds, socio-economic needs and the concept of different levels of aspiration should be considered and utilized. Stress on the importance of developing self realization would foster the growth of self confidence and a more willing acceptance of responsibility.

Today's major health problems are different, but they can be resolved as effectively by good school health programs as previous problems encountered in the past. Only unawareness, apathy, resistance to change, and, an indifference to the need for personal improvement will prevent this vital teaching that can eliminate ignorance about health fallacies and develop human potentials to the fullest capacity of the individual.

Joseph J. Bellizzi, m.d., *Chairman.*
Adv. Committee on School Health.

Endorsed by the Council, October 28, 1964.

The Abused Child

Reprint of C.S.M.S. news release of November 11, 1964.

The Connecticut State Medical Society is recommending to its 3,500 physician members that they voluntarily report cases of suspected child abuse to the State Health Department.

This action is being initiated following approval by the Society's governing Council of a proposal offered by its Committee on Public Health.

In making the announcement, Dr. William R. Richards, General Manager, said: "The plight of the abused or battered child is receiving more and more national attention. While it is true that the problem may first present itself as a medical situation, it is widely recognized that it is more often a social one—involving the community-at-large. Hospital personnel, teachers, clergymen, lawyers, family relatives and others all have an equal responsibility with doctors to report instances in which they believe children are being abused by parents or guardians."

"This recommendation of the Society is limited to 'voluntary' reporting by our members at the present time. At national and state levels, consideration is being given to enacting laws which would make such action mandatory. While we might ultimately support legislation of a mandatory nature, we do not believe it should be limited to reporting by physicians only, but should be extended to involve every Connecticut resident as a matter of civic duty. And because a private citizen can only report his 'suspicion' that a child has been abused, subject to confirmation by the authorities, we would naturally insist that proper protection against suit for libel or slander be made an integral part of any mandatory statute."

Letters To The Editor

TOWN AND GOWN

To The Editor:

Alarms have recently been sounded about the relationship between the university medical center and the community hospital and between consultants and referring physicians. The same standards of behavior must apply between all to ensure excellent medical care for our patients. Rumblings overheard at hospital coffee shops indicate that too frequently the referring physician has not been courteously treated at the "mecca" or by the well known consultant. The term, L.M.D. (local medical doctor) instead of invoking the image of the responsible physician desiring the best treatment for his patient even if it may mean loss of immediate patient supervision has been twisted to mean "country clod" by young house officers and junior attendings. "What, Mrs. Jones, wasn't a serum manganese level performed when you first saw your L.M.D., whazzis name?" Proper manners as well as proper ethics have not been employed. Too often the consultant fails to promptly inform the referring physician of his findings and never discusses with him a choice of a further consultant if this should be necessary. There have been instances where a patient has died while at a distant "mecca" and the referring physician is not immediately informed and learns of it only when a bereaved family calls him to find out why. These rare occurrences should be stamped out immediately and consultants should realize that they bear only minimal responsibility and share even this with the referring physician.

The referring physician also bears a major responsibility in providing the consultant with data that may help in his formulation. Clinical information of important value was supplied by the referring physician in only 53 per cent of one hundred consecutive patients referred for neurological evaluation. (1.) No information was supplied in 28 per cent of the referrals. It is of interest that information supplied by phone call was always pertinent and useful.

Good medical care demands consultation for assistance in resolving complex problems. The relationship between the consultant and the referring physician must be a warm, two way street where both respect each other's opinions and joint decisions must be made only after complete discussion and agreement. Face to face or telephone discussion will provide our patients with the best care.

REFERENCE

1. Kunkle, E. C.: Communication breakdown in referral of the patient. J.A.M.A., 187: 663, 1964.

William F. Eckhardt, Jr., m.d.

New Canaan, Conn.

To The Editor:

RE: CLINICAL MEDICINE, AUGUST ISSUE.

After spending the summer in New York and Connecticut, I have been trying to catch up on the reading matter which has accumulated during my absence.

When starting the article, I was amazed and shocked that anyone would artificially rupture the membrane, on a primipara, twelve hours after the first sign of labor and with the cervix dilated only 2 cm. I approved of all the comments but was again surprised that no mention was made of, what seemed to me, the cause of all the difficulty and the tragic ending.

During my early years of practice I delivered hundreds of women in their homes; never lost but one patient during childbirth; never did episiotomies and was obliged to repair very few lacerations. The one who, in 1918, died during childbirth was sick with influenza.

The amniotic fluid and sac have been provided by nature to protect the foetus and to facilitate birth. When the membrane remains intact, it precedes the head and exerts even pressure in all directions to dilate the cervix and birth canal.

I realize things have been speeded up in the last fifty years but I hope the young medics are not being taught to ignore the laws of nature and physics.

Very respectfully,

Wallace C. Douglass, M.D.

St. Petersburg Beach, Florida

Dear Dr. Douglass:

Your recent letter to Dr. Louis H. Nahum, Editor of Connecticut Medicine, has been referred to me for review.

Thank you for bringing to our attention the fact that we inadvertently failed to comment on the matter of rupture of the membranes in this situation. It seemed to the committee who published this article that there were so many gross errors made in the handling of this case, that commenting on the early artificial rupture of the membranes was not that important.

When there is a specific and urgent medical indication for induction of labor, artificial rupture of the membranes at 2 cm. dilatation seems to me to be a justifiable procedure if the head is deep in the pelvis. The information supplied in this case does not state the position of the head. Be that as it may, in an elective situation, you are more than correct concerning the ill-advisement of artificial rupture of the membranes in this case.

I wish to thank you again for your interest.

Sincerely yours,

C. D. Davis, M.D.

Professor of Ostetrics and Gynecology
Yale University School of Medicine

To The Editor:

A book—*Familiar Medical Quotations*—which we hope will be a great collection of wit and wisdom from and about physicians of the ages is being assembled. The writings and utterances of physicians, teachers and investigators from the dawn of medical history to the present are being sifted for the nuggets of genius and brilliant good humor which characterize the humanity of a profession. The collection will also include quotes from lay writers—including the scriptures—dealing with doctors, disease and medical life.

We are particularly anxious to obtain the quotations of individuals who, unlike Shakespeare and Osler, have hidden their occasional gems so that only a few are aware of them.

We welcome all such favorite quotes that your readers would like to see included in this volume. Contributions may be addressed to me c/o *Familiar Medical Quotations,* 34 Beacon St., Boston, Mass. 02106.

Sincerely yours,

MAURICE B. STRAUSS, M.D.
Editor.

Little, Brown and Company
34 Beacon Street
Boston 6, Mass.

Three Days Of Cardiology
January 21-23, 1965

"Three Days of Cardiology," a "Recognition of Coronary Artery Disease," will be held January 21-23, 1965 at Wayne State University, College of Medicine, in Detroit, Michigan.

The course, designed to discuss in a noninstructive way the current status for the recognition of arteriosclerotic heart disease, is being presented by The Council on Clinical Cardiology of the American Heart Association in cooperation with the Michigan Heart Association.

Discussions are grouped around the topics of clinical recognition of coronary artery disease, coronary arteriography, recognition of coronary artery disease by clearance methods, by radioisotopes and by apex vibrations.

"Three Days of Cardiology" is a series of postgraduate courses held several times a year in selected medical schools or medical centers throughout the country.

For further information please contact your local Heart Association.

Patronize Your JOURNAL

Advertisers

Manufacturer's Identity Needed On Drug Prescriptions

In writing a prescription, a physician should use the drug's trade name or the manufacturer's name to make sure the patient will receive the drug "in a form of highest quality and expected potency," according to an editorial in the current Journal of the American Medical Association.

"In most prescribing situations, a modified generic name or a brand name is necessary if the physician is to retain control over the source of supply," it said.

"Having decided that medication is required, he should assume the responsibility for selecting a manufacturer who will supply the drug in a therapeutically effective form at the lowest possible cost to the patient."

This can be done in one of three ways: by writing the generic name plus the name of a manufacturer known to be reliable, by writing the desired brand name, or by writing the generic name plus the desired brand name.

The generic term for a drug is an appropriate chemical name and is necessary for effective teaching and communication among physicians, the editorial explained. Brand names are put on a drug by the manufacturers some time after the generic name is assigned.

Physicians should recognize that use of generic names is "solely for educational purposes," the editorial advised, adding:

"When a physician uses a brand name or a manufacturer's name to designate the source of supply, he is fulfilling a part of his professional obligation to his patient."

Corrective Lenses Impractical In Wraparound Sunglasses

It is not feasible to put corrective lenses in wrap around sunglasses because of the induced astigmatism in glasses so large and so extensive in curvature, according to a consultant to the Journal of the American Medical Association.

Writing in the current J.A.M.A., Dr. John A. Dyer, Rochester, Minn., added that good quality wraparound sunglasses made of molded plastic cause virtually no distortion

"Those of cheap quality do produce some distortion because of the irregular surface and varying density of the plastic material but even they have proven to be quite satisfactory for outdoor sports activities," he said.

OBITUARY

Thacher W. Worthen, M.D.

1886 - 1964

Dr. Thacher Washburn Worthen of 183 Bloomfield Avenue, Hartford, Connecticut, a member and past president of the surgical staff of Hartford Hospital, died on September 9, 1964 at Hartford Hospital after a short illness.

Born in Woodstock, Vermont, he was a graduate of Dartmouth Medical School, Hanover, New Hampshire, Class of 1911. He served his internship and residency at the Nursing and Children's Hospital and Women's Hospital in New York City and at the University of Tupingin, Germany from 1914 to 1915.

He served in the Army Medical Corps until he came to Hartford Hospital in 1918, where he became a member of the hospital's medical and surgical staff and served as its president from 1948 to 1950. At the time of his death, he was a member of the honorary medical staff at the hospital.

He was a fellow of the American College of Surgeons, the New England Surgical Society, the American Board of Surgeons, the Hartford Medical Society, past president and chairman of the board of directors and chairman of the building committee of the Hartford Medical Society, a member of the American Medical Association, and the Connecticut State Medical Society.

He was a consulting surgeon at the Institute of Living, Mt. Sinai Hospital and Bristol Hospital, Bristol.

He leaves his wife, Mrs. Mary Welles Paine Worthen; a son, Frederick P. Worthen of Andover, Mass.; three daughters, Mrs. William Runyon of Augusta, Maine; Mrs. Robert Morton of Sunset Farms, West Hartford; and Mrs. Thomas Hall of South Shaftsbury, Vermont, and fifteen grandchildren.

Freeman P. Clason, M.D.

In Memoriam

Fabricant, Samuel E. — Waterbury; Jefferson Medical College, 1919. Dr. Fabricant was on the medical staffs of the Waterbury and St. Mary's Hospitals. He was a member of the Waterbury Medical Association, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Fabricant died October 22, at the age of 67.

Genovese, Serafino—Danbury; Cornell Medical College, 1911. Dr. Genovese was a skin specialist in the Danbury area for over twenty years. He was an instructor in dermatology at Polyclinic Hospital in New York City for many years. A former member of the New York Academy of Medicine, he was certified by the American Board of Dermatology and Syphilology in 1939. Dr. Genovese was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Genovese died October 24, at the age of 76.

Greenspun, David S.—Bridgeport; Yale University School of Medicine, 1925. Dr. Greenspun served in the United States Army Medical Corps as Captain from 1942 to 1945. He was a Fellow of the American College of Physicians and a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He had served as President of the Connecticut Chapter, Arthritis and Rheumatism Foundation. Dr. Greenspun died October 14, at the age of 65.

Lerrick, Alan — Fairfield; State University of New York College of Medicine, 1946. Dr. Lerrick served with the U. S. Army and Air Force Medical Corps, was editor of Air Surgeon's Bulletin, and an advisor on production of medical motion pictures for the Army Medical Corps. Dr. Lerrick was a surgeon at both the Bridgeport and St. Vincent's Hospitals, and he was on the faculty at Yale University School of Medicine. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Lerrick died October 25, at the age of 41.

NEW BOOKS IN REVIEW

SYNOPSIS OF PATHOLOGY, 6th Edition. By W. A. D. Anderson, M.A., M.D. The C. V. Mosby Company, St. Louis, Missouri, 1964, 839 pp., 406 text illustrations, 4 color plates. $9.75.

Reviewed by: LOUIS H. NAHUM

This handbook attempts to present pathology in a compact concise and also comprehensive form. It is aimed toward the medical student and dental student who are studying pathology but also to the clinician who needs a handbook to remain familiar with one of the fundamental sciences in medical practice. It is simple enough to interest those who are in the paramedical fields who need some knowledge of disease processes.

Since the last edition there has been a resurgence in our knowledge of cellular function and morphology, electron microscopy, cytochemistry, virology, genetics and cytologic studies of cancer, and these have revealed many facets of the cellular basis of disease processes unknown a few years ago.

In the 25 chapters, we find a conventional arrangement—inflammation, infections, poisons, nutritional disturbances, disturbances of growth, as well as all organs and systems. Many of our newer concepts have yet to be covered in the next edition. For example, in the complications of myocardial infarction, fatal arrhythmias are not mentioned, though they account for one-quarter of fatalities in the acute stage. Acute lymphocytic leukemia is now known to arise in the thymus, not in the bone marrow. The function of the thymus is known not unknown as is stated. The importance of vascularization of the atherosclerotic plague as a serious cause of obstruction is not brought out. Obstruction of the lymphatics of the heart as a cause of certain obscure forms of heart disease is not mentioned, etc.

On the whole, the book is a guide to the reader but the field is expanding so rapidly that he must check with current literature to be sure the conventional concepts are still acceptable not outdated.

DYNAMIC PATHOLOGY: STRUCTURAL AND FUNCTIONAL MECHANISMS. By Maurice M. Black, M.D. and Bernard M. Wagner, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1964, 281 pp., illustrated. $8.00.

Reviewed by: LOUIS H. NAHUM

This little book can make us aware of dynamics in pathology. It has a philosophy, namely that pathology should seek to define the nature and consequences of those structural and functional aberrations which we term pathological and which commonly have their classical expression in overt disease. Without doubt such knowledge is basic to any rational approach to the diagnosis, treatment and prevention of disease.

In this book is emphasized the thread of continuity which runs throughout medicine in general and pathology in particular. It gives a glimpse of the broad vista—that pathology can be a foundation of medical investigation and practice. It consists of two parts: homeostatic mechanisms dealing with concepts and terminology, cells, genetics and development, vascular homeostoses, the reticuloendothelial system, endocrine homeostasis, hepatic homeostatic function, renal homeostatic function and connective tissue, are in the first part; Part two deals with challenges to homeostasis such as neoplasia, ionizing radiation, deficiency disease, infectious disease and aging.

Altogether, we are presented the synthesizing point of view that disease may be viewed as derangement in homeostasis and that the pathologist is concerned with the recognition and understanding of the structural and functional consequences of such changes. We see that biological systems are orderly and susceptible of understanding. To those who become mired in the morass of infinite details seemingly unconnected, when consulting a hand-book or even a text-book of pathology, one gains in this beautifully conceived and executed book a sense of beauty and excitement when pathology is presented in a dynamic aspect. Student and practitioner of medicine will use this book as a philosophy of pathology; teachers as an illuminating technique to make pathology teaching fruitful, meaningful and inspired.

ADVANCES IN METABOLIC DISORDERS. Volume I. Edited by Rachmiel Levine and Rolf Luft. Academic Press, New York, 1964, 366 pp. $12.00.

Reviewed by: PHILIP K. BONDY

This volume consists of a series of essays on the present status of knowledge in a variety of fields. It includes a discussion of Glycogen Storage disease by Hers, the Parathyroids by Aurbach and Potts, Mitochondrial Respiratory Control by Ernster and Luft, Osteoporosis by Nordin, the Thyroid Hormones and the Basal Metabolic Rate by Tata, Insulin Antagonists and Inhibitors by Vallance-Owen, Aldosterone by Laragh and Kelly, and Folic Acid Deficiency in Man by Luhby and Cooperman. Each essay is self-contained and authoritative, since the authors are all experts in their fields. For the most part the material is presented in a balanced fashion which gives fair expression to all sides of current controversies; however, Hers' discussion of the glycogensis rests rather more heavily on the concept of a single enzyme defect than is acceptable to some clinicians. The editors have selected subjects which are still in flux, so it is predictable that certain aspects of each discussion already appear a little out of date. The book must be read as a summary of the state of rapidly altering knowledge at a point in time. Such a summary is useful to the degree that it offers the reader assurance that the problem has been completely summarized, and that the pertinent references are available. The essayists in this volume do a good job of summarizing the development of present thoughts, and of presenting a well-selected sampling of the literature. The book will be of value to anyone interested in correlating basic science with present problems in the areas under discussion, and will be helpful to students and research workers seeking a current and complete summary of these problems.

THE LIVER AND PORTAL HYPERTENSION. By Charles G. Child III, M.D. Volume I in the Series: MAJOR PROBLEMS IN CLINICAL SURGERY. W. B. Saunders Company, Philadelphia, Pennsylvania, 1964, 225 pp., illustrated. $8.50.

Reviewed by: JAMES R. CULLEN

This book has a dedication to the memory of Allen O. Whipple, B.S., M.D., Sc.D., by Louis Rousselot, M.D., and a foreword by J. Englebert Dunphy, M.D., Consulting Editor, which gives a background on the history of advances in liver disease and portal hypertension and explains the purpose of this book, which is to bring to the practicing surgeon, a timely and all-inclusive report of the "basic concepts and technical approaches to the study and treatment of portal hypertension." It represents a clear picture of liver disease and its pathological states by a leading group in this field and will be of great help to all who treat these conditions.

There are seven chapters occupying 225 pages under the headings of: Surgery and Portal Hypertension; Some Aspects of Hepatic Failure; Hepatic Encephalopathy; The Liver and Protein Metabolism; Salt, Water and Adrenal Steroid Metabolism; Liver Lymph, a Critical Component of Hepatic Cirrhosis; and Experimental Surgery of the Portal Vein, Hepatic Artery and Hepatic Vein. Several authors contribute to these various chapters, and present a most complete and interesting documentary in their special fields.

To anyone interested in the surgery of portal hypertension, the first chapter on Surgery and Portal Hypertension, and the last chapter in Experimental Surgery of the Portal Vein, Hepatic Artery and Hepatic Vein, will prove very worthwhile. They are easily understood due to conciseness in the written material and through excellent pictures and drawings which illustrate the text in the clearest manner possible. The bibliography is extensive throughout the book, there being 143 references alone for the first chapter.

The authors state that their purpose in writing this book is to aid physicians, pediatricians, and surgeons in rendering the best medical and surgical care to patients afflicted with the complications of abnormal elevations in portal pressure and I believe they have admirably accomplished their objective. This book is a must for all physicians treating these conditions, and I strongly recommend it as a most interesting and up to date treatise on liver disease and portal hypertension.

CORNEAL CONTACT LENSES. Edited by Louis J. Girard; Joseph W. Soper and Whitney G. Sampson, Associate Editors. C. V. Mosby Company, St. Louis, Missouri, 1964, 329 pp., illustrated. $19.75.

Reviewed by: R. M. FASANELLA

This text is produced by members of the Contact Lens Section, Department of Ophthalmology, Baylor University College of Medicine, Houston, Texas.

It is estimated that eight million persons in the United States wear contact lenses yet although contact lenses were invented over a hundred years ago, only in 1948 did the invention of plastic corneal contact lenses "come to stay."

Reluctantly, though in many cases they did fit contact lenses, ophthalmologists came to realize that they had to play the important role of supervising the care of the large numbers of their patients wearing contact lenses.

This text is written so that the ophthalmologist can handle every aspect related to the fitting of corneal contact lenses. Optics, corneal metabolism, indications, and contraindications plus the management of routine and complex problems are thoroughly covered.

The text material is easy to follow and illustrations, particularly the line drawings, are beautifully clear.

Although the book is meant prinicpally for the ophthalmologist, it should prove of interest to optometrists, opticians and physicians whose patients and families wear contact lenses and who want helpful, authoritative up-to-date information on this subject.

IN VIVO. By Mildred Savage. Simon and Schuster, New York, 1964, 639 pp. $5.95.

Reviewed by: ORVAN W. HESS

Occasionally important aspects of medicine are recorded in a literary form using essentially non-technical language. In medical libraries writing in this technique is considered quite unorthodox. Yet the impact of this variety of literature, like Arrowsmith, can be great. The paucity of accomplishment in this art form, so badly needed to bridge the existing gulf of understanding between men of Science and of the Humanities, has been emphasized by Sir Charles Snow. *In Vivo,* as a science novel by a Connecticut author, aids in lessening this gap. Mildred Savage's book deals in depth with the complexities, trials and frustrations of research albeit in this instance by a team of scientists in industry. The writer has provided, after years of personal investigation, a factual record of the drama surrounding the search for and implementation of a new wonder drug. With perceptive insight of almost psycho-analytic quality, the lives and motivations of a group of men and women involved in this exciting adventure are woven by the author into a tale of sustained interest and suspense. *In Vivo* provides a window through which those engrossed in non-medical pursuits may get a glimpse of the nature of the research scientist and the complex interrelationship to forces within society which aid and abet his efforts. Those oriented with medical research, standing more closely, may be confronted with a reflection of experience not unlike their own. This book is highly recommended for entertainment as fiction dramatizing science and for its significance as an historic novel recording an important phase of medical progress.

INFECTIOUS DISEASES OF CHILDREN. By Saul Krugman, M.D. and Robert Ward, M.D. C. V. Mosby Company, St. Louis, Missouri, 1964, 423 pp., 8 color plates. $15.75.

Reviewed by: CHARLES A. WOODS

With the third edition the authors have brought up to date their superb book on infectious diseases in children. The book very ably accomplishes its purpose, as was stated in the preface to the first edition, "to provide a concise and handy description of certain common infectious diseases of children."

Although the format is similar to the last edition each chapter has been revised and new information added. There is included information on the live measles vaccine and other new immunizing agents and recommendation for their use. A new chapter on cytomegalovirus infections has been added. The common upper respiratory infectious agents are considered together in a very informative chapter which covers both the clinical syndromes and the etiologies.

The print style has been changed slightly which makes the book even more readable. There is present, as in the previous edition, a limited number of excellent color prints.

1965 MEETINGS

March 18—181st Annual Meeting of the New Haven County Medical Association to be held at the Waverly Inn, Cheshire, Connecticut beginning at 2:30 p.m.

April 27-29—Connecticut State Medical Society Annual Meeting to be held at Statler-Hilton Hotel, Hartford, Connecticut.

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Doctor's Office

C. Thomas Chiaramonte, M.D., announces the opening of an office for the treatment of skin diseases at 1 Padanaram Road, Danbury.

Larry Edwards, M.D., announces the removal of his office for the practice of ear, nose, throat, and plastic surgery to Heritage Square, 1700 Post Road, Fairfield.

Edward R. Harvey, Jr., M.D., announces the reopening of his office for the general practice of medicine and surgery at 119 Main Street, Seymour.

Sidney W. Jennes, M.D., announces the removal of his office for the practice of allergy to 1389 West Main Street, Waterbury.

Donald McKay, M.D., announces the opening of an office for the practice of surgery at Railroad Avenue, Essex.

Gerald O. Strauch, M.D., announces the opening of an office for the practice of general surgery at 1116 Summer Street, Stamford.

Charles Noyes Sullivan, M.D., announces the removal of his Bloomfield office for the practice of dermatology to 820 Park Avenue, Bloomfield.

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*Clinical report on file, Medical Department, A. H. Robins Co., Inc.

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Mental Problems Greater At Commuter College

Mental problems appear to be greater among "commuter colleges" students than among those attending residential schools, according to Dr. John E. Kysar, Chicago.

Dr. Kysar reported on his five years' experience as psychiatric consultant at the Chicago Undergraduate Division of the University of Illinois in the current Archives of General Phychiatry, published by the American Medical Association.

The university branch, located in the heart of Chicago, has 5,000 full-time students, 99 per cent of whom commute daily from home.

Although statistical comparisons are not possible, Dr. Kysar said his experience suggests that there is a "higher rate and more severe psychopathology in the student population of this commuter school as compared with most residential schools" and this may be true generally at other urban commuter universities.

He attributed the higher rates to three large groups in the student body—those from unstable or broken homes; those from families of lower socioeconomic status, which studies indicate carries a progressively larger risk of impaired mental health during adulthood; and those who have "individual pathology" related to their selection of the commuter school.

While there is no doubt that students from low-income families enter the commuter school largely because of financial limitations, Dr. Kysar said, there are a surprising number whose families have sufficient means to help them to go to a residential school.

Among these commuter-by-choice students, he found that feelings of inadequacy, overcontrol of impulses, isolatedness, indecision, social-sexual maladjustment, and dependency and conformity to parent's expectations were prominent characteristics.

According to some studies, Dr. Kysar pointed out, vulnerability to mental disorder results from damaging events in childhood or early adulthood, such as separation from a parent by divorce, death, or illness; and unstable family situation in which one or both parents may be alcoholic, criminal, mentally ill, or in marital disharmony; and crossing from one social or cultural setting to another markedly different one producing "cultural shock."

These factors were seen more commonly among commuter students than among residential students, the Chicago psychiatrist said.

The greater prevalence of mental health problems among commuter students implies that the need for preventive health measures is greater in the commuter university than in the residential school, Dr. Kysar maintained.

Yet in the commuter university, he said, mental health facilities have been largely neglected on the assumption that if the student is living at home, his family will provide for his health needs and will utilize community health services as necessary. This is often an erroneous assumption, particularly in the mental health area, he added.

Dr. Kysar proposed a mental health program in the commuter school which would offer individual and group psychotherapy. Short-term counseling with parents also would be advantageous, he said. Since there are common problems among these students, such as isolatedness and social inadequacy, he added, it is quite possible that a better response might be obtained through social psychiatric methods. He suggested a concerted effort to include every student in some growth-promoting extracurricular group which would enhance his psychosocial development along with his intellectual development.

It should be remembered that the commuter student has more strengths than his peers who do not enter college, Dr. Kysar added, and the potential for change and improvement in the college group is believed to be remarkably high.

Perhaps nearly half of the four million students in college today attend commuter schools, it was pointed out. At the Chicago school, men outnumber women three to one, a common finding in large public commuter schools.

Dr. Kysar cautioned that his findings do not indicate that the entire student population of the Chicago school or other nonresidential schools is made up of students whose mental health is impaired or who have been exposed to trauma or deprivation. There are not only some students whose mental health may remain unimpaired in spite of stressful experiences, he said, but also some students whose selection of the commuter college is not primarily motivated by pathological factors.

AMA Research Institute To Open July 1, 1965

The Biomedical Research Institute of the American Medical Association Education and Research Foundation will open July 1, 1965, AMA-ERF Board President Raymond M. McKeown, M.D., Coos Bay, Oregon, announced recently.

Headquarters for the institute will be located in a new addition to the AMA headquarters building. The project, now under construction, will include about 30,000 square feet of laboratory space.

McKeown also announced the appointment of a fifth member of the Committee of Scientific Advisors to the Biomedical Institute. He is Henry Eyring, Ph.D., a chemist and dean of the Graduate School at the University of Utah, Stalt Lake City.

Eyring, who is president-elect of the American Association for the Advancement of Science, has conducted extensive research in the fields of radioactivity, application of quantum mechanics to chemistry, theory of reaction rates, and theory of liquids.

The other members of the committee are William Hugh Feldman, D.V.M., chief of laboratory research in pulmonary diseases for the Veterans Administration, Washington, D. C.; Chauncey D. Leake, Ph.D., Department of Pharmacology, University of California School of Medicine, San Francisco; D. D. Van Slyke, PhD., member-emeritus of the Rockefeller Institute, New York City; and Maurice B. Visscher, M.D., distinguished professor of physiology, University of Minnesota, Minneapolis.

McKeown said the advisors will submit advice about potential and prospective members of the research institute, and consider relevant scientific questions in the area of molecular biology.

In its first official act, the AMA-ERF Board delineated the purposes and policies of the institute. There are:

"1. To provide appropriate personnel, facilities, and conditions, conducive to obtaining significant, basic biomedical information which eventually may be applied to promoting the good health of people.

"2. The personnel, nominated by the Committee of Science Advisors, will include biomedical scientists of the best possible stature or promise with which such secretarial and technical assistance as may be appropriate to their respective activities, and with such post-doctoral fellows as may be provided for by the individual investigators in relation to their facilities and wishes.

"3. Initial laboratory facilities will include 30,000 square feet of space to be set up and equipped on the recommendations of the scientific personnel and the Committee of Scientific Advisors, together with appropriate quarters and care for experimental animals. Extensive library facilities will be available through the headquarters organization of the American Medical Association.

"4. Every possible effort will be made to establish such conditions in the institute as will be stimulating for biomedical investigation in accordance with the highest scientific standards and ideals. The organizational policies of the American Medical Association provide liberal financial security and prerequisites. Responsible freedom in research and publication is assured. The Committee of Scientific Advisors is expected to maintain the best possible intellectual environment for supporting investigation into basic and fundamental biomedical scientific problems."

Study Indicates Body Build Predisposes To Obesity

A study of obese adolescent girls indicates that body build, and hence genetic factors, are a predisposing factor in obesity.

Among 180 girls, most of whom were aged 12 to 17, all but 5 were predominantly endomorphs, Carl C. Seltzer, Ph.D., and Jean Mayer, Ph.D., Harvard Universtiy School of Public Health, Boston, reported in the current Journal of the American Medical Association.

The endomorph has a roly-poly physique with the abdomen larger than the chest and relatively small hands and feet.

"Presumably, the prime prerequisite for the development of obesity is a physique with at least a moderate amount of endomorphy under normal nutritional conditions," the researchers said. "Endomorphy predisposes to the laying on of fat unless insufficient diet, excessive activity, disease, or voluntary weight control supervenes."

However, they added that even among endomorphs there is considerable individual differences in the tendency to accumulate fat and not all endomorphs become obese.

"While these results in no way detract from the concept that caloric intake in excess of caloric expenditure is the immediate cause of abesity, a recognition of the constitutional individuality of the person may well give a greater understanding of the common observation that, under similar environmental circumstances, some of us become obese and others do not," the researchers commented.

The findings, they stressed, may not hold true for adult obese men and women, or perhaps even obese adolescent boys.

"In adults, particularly, the problem is much more complex since one must deal with those physical types which are prone to a sudden blossoming into middle-age obesity," they pointed out. "Any study of adults, therefore, must distinguish between those whose obesity is long standing, going back to childhood and adolescence, and those whose obesity is a singular characteristic of midlife."

The authors said they believed endomorphy would still predomonate among the overweight girls studied even if they shed enough fat to be of normal weight for their age, sex, and height, although final proof would rest on lengthier studies.

The study also uncovered a somewhat greater tendency to mesomorphy among the obese girls than is found among girls of similar ages in the general population. The mesomorph has a larger chest than abdomen, is muscular and has prominent body joints.

On the other hand, there was an extremely low rate of ectomorphy, the lanky physique with delicate bony structure and stringy muscular development.

"Not only are our abese subjects less ectomorphic than the general population or even the highly endomorphic elements of the general population, they also reflect the total absence of a wide variety of ectomophic physical types," the researchers commented. "Apparently, nature is intolerant of obesity in ectomorphic types."

Those in the study group, aside from being overweight, were apparently healthy. Most were girls attending a summer weight-control camp (Camp Seascape, East Brewster, Mass.), while others were seen at the out-patient clinic of the Adolescent Unit of Children's Hospital Medical Center, Boston.

"Genetic factors are known to play an important role in the development of obesity among experimental animals, yet . . . relatively little attention has been focused on the genetic factors in the development of obesity in humans," according to an accompanying editorial in the Journal.

"Granted that typing of obesity is at its very infancy in humans, it appears reasonable to think that only when distinct syndromes resulting in prolonged positive energy balance have been identified and their pathogenesis understood will it be possible to treat obesity 'in depth' rather than merely to manipulate food intake and exercise to establish a negative energy balance.

"The preliminary work of Seltzer and Mayer may well lead to the early identification of those predisposed to slimness as well as obesity. With observations showing the familial—and probably genetic—character of the predisposition to obesity, their study should lead us to look at obesity as a medical rather than a moral problem, and regard the obese person as a victim of anatomic and physiologic circumstances rather than as just a glutton."

Dr. Seltzer is a research associate in physical anthropology and Dr. Mayer is an associate professor of nutrition.

Improved Ultrasonic Device Used For Meniere's Disease

Improved ultrasonic equipment used to treat 65 patients with Meniere's disease, a disorder of the inner ear causing attacks of dizziness, relieved symptoms completely in 80 per cent.

The use of a "new and technically reliable" ultrasonic generator at Columbia Presbyterian Medical Center, New York City, was discussed in an editorial in the current Journal of the American Medical Association.

"There appears to be a significant increase in the number of patients suffering from Meniere's disease," the editorial said. "There is some evidence that strain and stress of day-by-day affairs have contributed to the rising incidence of this disease."

Until recently the only effective treatment was surgical destruction of the inner ear, which resulted in deafness in the treated ear.

Ultrasound, or the energy produced by high frequency sound waves beyond the audible range, can selectively destroy that part of the inner ear, responsible for the symptoms of the disease, and hearing is preserved, according to the editorial.

The technique, introduced in Europe in 1952 for Meniere's disease, was described by Drs. Milos Basek and V. N. Epanchin, College of Physicians and Surgeons, Columbia University, in the current Archives of Otolaryngology, published by the AMA.

High frequency sound waves, produced by a generator, are focused through a pencil shaped instrument into a narrow straight beam of energy. This energy, amounting to less than one watt, is directed to the labyrinth of the inner ear, which contains the sense organs of equilibrium, for about 20 minutes to destroy the activity of the labyrinth.

Numerous difficulties were encountered with previous ultrasonic equipment, the physicians pointed out. The biggest problem associated with the use of ultrasound for this disease is the possibility of damaging the facial nerve and causing mild paralysis, they said.

The generator used in this series of patients, which was made in Australia by George Kossoff, a physicist, is safe and efficient, the researchers said. For a skilled operator, the device is not difficult to use. The danger of facial nerve paralysis is less than five per cent and if paralysis occurs, it disappears in a few weeks without additional treatment.

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County Activities

At a recent Board of Director's meeting of the Auxiliary to the Connecticut State Medical Society several counties reported on their plans for raising money for scholarship funds and on their community activities—which should help to answer the question "Why An Auxiliary?"

Windham County held an "Evening of Music" with duo-organists, Helen Henault and Timothy Storrs, at the Pomfret Community School on Saturday October 3. $465 was netted for the fund.

As a community project the Auxiliary initiated a "Pre-school Visual Screening" clinic which was lauded at the Fall Conference of the A.M.A. Auxiliary and received an award for meritorious community service from the Connecticut Society for the Prevention of Blindness. This project is concerned primarily with the detection of weakness in one eye causing overuse of the other eye, at an early age when corrective measures are most effective.

Fairfield County held a dinner dance on November 14 at the Darien Country Club. Proceeds have not yet been announced.

The Auxiliary members are at present conducting a poll of the community services in which they are participating, such as Red Cross, Hospitals, United Fund, etc.

Middlesex County held a Ball at the Hotel America in Hartford on November 28. Proceeds from this event will be announced at a later date.

Middlesex County Auxiliary members have been working as volunteers at the Connecticut Valley Hospital during visiting hours. More volunteers are being sought to help during the recently extended visiting hours. Also birthday cakes have been contributed by members and more are desperately needed so that each patient may have one on his birthday. These can be delivered at any time since they are stored in the freezer until needed.

New Haven County is planning to make an annual event of the Burgundy Ball which proved to be so successful last year. The 1964-5 "Ball" is scheduled for March 6, 1965 again at the Yale Law School.

Auxiliary members have started a "Coffee Hour" at the Veteran's Hospital. Their first assignment was in a ward of mental patients. At present volunteers are covering one afternoon a month. It will be possible to extend this service when more volunteers are available.

A.M.A.-E.R.F. chairmen in all the counties are busy displaying and selling these Christmas cards as well as charms, writing paper, and playing cards for the benefit of the Auxiliary contribution to the student loan fund of A.M.A.-E.R.F.

The Bulletin

Have you noticed a new periodical in your home titled "BULLETIN OF THE WOMAN'S AUXILIARY?" All Auxiliary members are now receiving this magazine through the courtesy of your A.M.A. It is not really new, but now it looks like a magazine rather than an official document and *every* member receives it, not just those who subscribe to it. It's aim is to be both informative and interesting. Comments will be appreciated.

AROUND THE STATE

New Haven County

The 181st Semi-Annual Meeting of the New Haven County Medical Association, Inc. was held on Thursday, October 22, 1964 at the Waverly Inn, Cheshire, with Dr. Jack Galen, President, presiding.

The necrology was read by the clerk while the audience remained standing. The names of ten members were recalled.

Dr. Ralph Gilman, President of the Connecticut State Medical Society was introduced, to be followed by other State Society officers, notables and the delegates from Litchfield and Hartford counties.

Items of interest included interim committee reports, establishment of a budget, including dues, election of thirty-nine new members (two by State transfer) of a Nominating Committee, report of the By-Laws Revision Committee, a new non-medical health insurance plan, and a report by the President of the New Haven County Hospital Association by Dr. Waldo E. Martin of Milford.

The meeting adjourned to a social hour followed by dinner. During the evening recently elected new members were introduced and called forward to sign the register of membership.

Dr. Stewart J. Petrie, Program Committee Chairman then introduced Mr. John Lupton, Executive Director of the State Republican Campaign Committee who spoke on "Predicted Political Trends in 1965."

It is unfortunate that there had to be competition with other meetings, in spite of our date posting in Connecticut Medicine these past several months.

Respectfully submitted,
H. A. Levin, m.d., *Clerk.*

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Traumatic Cervical Syndrome And Whiplash. By Charles W. Goff, M.D., John O. Alden, M.D., and John H. Aldes, M.D., J. B. Lippincott Co., Philadelphia and Montreal, 1964, 124 pp., 48 plates and 135 illustrations, $5.00.

Clinical Neurology. By Frank A. Elliott, M.D., F.R.C.P., W. B. Saunders Co., Philadelphia and London, Oct. 12, 1964, 688 pp., Illustrated, $12.50.

Preventive Medicine in World War II, Volume VII, Communicable Diseases. Arthropodborne Diseases Other Than Malaria. Prepared and published under the direction of Lt. Gen. Leonard D. Heaton; Editor in Chief: Col. John B. Coates, Jr.; Editor for Preventive Medicine: Ebbe C. Hoff, Ph.D., M.D.; Assistant Editor: Phebe M. Hoff, M.A., Office of Surgeon General, Dept. of Army, Washington, D. C., 1964, 370 pp., Illustrated.

Hypertension-Blood Pressure And Toxemia Of Pregnancy, Volume XII. Proceedings of the Council for High Blood Pressure Research, American Heart Association, Cleveland, Nov. 15 & 16, 1963. Edited by Simon Rodbard, M.D., American Heart Assoc., Inc., N. Y., 1964, Illustrated, $2.50.

Pediatric Neurology. By 13 Authors. Edited by Thomas W. Farmer, M.D., Professor of Neurology, University of North Carolina School of Medicine, Chapel Hill. Hoeber Medical Division, Harper & Row, Publishers, New York, Evanston and London. 658 pp. with 189 illustrations. $18.50.

The Allergic Child. Edited by Frederic Speer, M.D., Assistant Clinical Professor of Pediatrics and Chief of Pediatric Allergy Clinic, University of Kansas School of Medicine, Kansas City, Kansas; Chief of Pediatric Allergy, Children's Mercy Hospital, Kansas City, Missouri. Hoeber Medical Division, Harper & Row, Publishers, New York, Evanston and London. 586 pp. with 132 illustrations, 14 in full color. $16.50.

Ciba Foundation Colloquia On Endocrinology. Volume 15. Aetiology of Diabetes Mellitus and its Complications. Edited by Margaret P. Cameron, M.A. and Maeve O'Connor, B.A., Little, Brown and Co., Boston, 1964. 405 pp. with 85 illustrations. $12.50.

Brain-Thyroid Relationships. With special reference to thyroid disorders. Ciba Foundation Study Group No. 18. Edited by Margaret P. Cameron, M.A. and Maeve O'Connor, B.A., Little, Brown & Co., Boston 1964. 117 pp. with 28 illustrations. $1.95.

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Supplement to CONNECTICUT MEDICINE, February, 1964

DOCTOR'S HOUSE CALL

by James Rogers Fox, M.D.

From the Studios of WBMI-FM (Dial: 95.7)
Meriden, Connecticut

Time: 1:55 P.M.
Daily—Monday through Friday

A Health Education Service by the Connecticut State Medical Society Public Relations Division

JAMES ROGERS FOX, M.D.

"Doctor's House Call," a series of 5-minute taped radio features, is sponsored by the Connecticut State Medical Society in the interest of health education. Dr. Fox, author and narrator of the series, is a practicing physician and member of the medical faculty of the University of Minnesota. He is a broadcaster of long experience and is Chairman of the Radio and Television Committee and Health Education Committee of the Minnesota Medical Society.

In addition to Dr. Fox's talk, each program carries a message about the activities of the State Medical Society and its component county associations. Frequent messages are also being aired to inform listeners about the Kerr-Mills program in Connecticut to finance health care for those over 65 who need help.

The American Medical Association's Advisory Comittee for Radio, Television, and Motion Pictures has endorsed "Doctor's House Call" and has reviewed each episode.

FEBRUARY	10	Accidental Poisoning of Children
	11	Medical Quackery
	12	Infectious Hepatitis
	13	Special Diets
	14	Growths on the Body
FEBRUARY	17	Overweight Troubles
	18	Overweight and Blood Pressure
	19	Age and Physical Activity
	20	Your Heart and Smoking and Alcohol
	21	Routine Heart Evaluations
FEBRUARY	24	Spot on the Lung
	25	Special Heart Examinations
	26	Bursitis
	27	Hemorrhoids
	28	Evaluation of an Allergy
MARCH	2	Difference of "Eye" Doctors
	3	Use of Common Drugs
	4	Health Tips and Water Activity
	5	Menopause and Hormones
	6	The Automobile and Your Health
MARCH	9	Hives
	10	Rheumatic Fever
	11	"Self-Prescription"
	12	"Rest" as a Health Measure
	13	Cold and Painful Hands and Feet
MARCH	16	Strokes
	17	Nasal Septum
	18	Intravenous Therapy
	19	Children's Emergency Procedures
	20	Balance (ear)
MARCH	23	Blackout
	24	Bowel Obstruction
	25	Numbness and Coldness of Hands
	26	Plantar Warts
	27	Low Back Pain Treatment
MARCH	30	Perygium and Cholesterol Placques
	31	Low Blood Pressure
APRIL	1	Skin Reactions
	2	Convulsions
	3	Sebacious Cysts
APRIL	6	Conjunctivitis
	7	Prevention of Rheumatic Fever
	8	Removal of Wax from Ears
	9	Sedation Changes of the Skin
	10	Kidney Stones

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SEPTEMBER	7	Pain and Arthritis
	8	Our Aging Joints
	9	Remedies and Nostrums
	10	Rheumatoid Arthritis
	11	Underweight Advantages
SEPTEMBER	14	Physical Activity Following Surgery
	15	Eye Defects in Children
	16	Various Types of Physical Examinations Part 1 Screening
	17	Various Types of Physical Examinations Part 2 Complete and Comprehensive
	18	Treatment of Heart Leakage
SEPTEMBER	21	Shortness of Breath Part I
	22	Shortness of Breath Part II
	23	Emergency Call to a Physician
	24	The Doctor's Medical Bag
	25	Accreditation of a Hospital
SEPTEMBER	28	Teen Age Fads
	29	Another Doctor's Opinion
	30	Common Tests
OCTOBER	1	Special Tests
	2	Changing Concepts in Hospital Care
OCTOBER	5	Attitude Toward Health
	6	Your Responsibility for Immunization
	7	Hazards of Transfusion Therapy
	8	What a Patient's Dentist Need Know
	9	Problem of Canker Sores
OCTOBER	12	Cancer Spread
	13	Coronary Terms
	14	Respiratory Infection Locations
	15	Repeated Head Injuries
	16	Eye Examinations
OCTOBER	19	Pains as a Symptom
	20	Peptic Ulcer
	21	Discussing Your Doctor's Charges
	22	Personal Eye Care
	23	Use of Wonder Drugs for Colds
OCTOBER	26	Colitis Care
	27	Menstrual Cycle Variations
	28	Hypertension
	29	Wry Neck
	30	Painful Swallowing
NOVEMBER	2	Rashes
	3	Physical Evaluation for Athletes
	4	Tiredness of High Altitude
	5	Cough Care
	6	"Athletes" Heart
NOVEMBER	9	Contagious Aspect of Infectious Hepatitis
	10	Resistance to Infection
	11	"Stomach Flu"
	12	Salt Free Diets
	13	Care of Nails
NOVEMBER	16	Purchasing Toys
	17	Immunization in Catastrophe
	18	Detecting Hardening of Arteries
	19	Your Precious Health
	20	Treatment of Angina
NOVEMBER	23	Heart Sack
	24	Labrynthitis
	25	Nervous Habits Indicating Tension
	26	Soft Spots in Baby's Head
	27	Floating Blood Clots
NOVEMBER	30	Inhaling Fumes for "Kicks"
DECEMBER	1	The Church Dinner "Hepatitis"
	2	Testing for Hearing
	3	Tests for Thyroid Function
	4	Treatment of Temper Tantrums
DECEMBER	7	Cancer Precursors
	8	Cancer Evaluations
	9	Industrial (Occupational) Medicine
	10	Exams Used in Occupational Medicine
	11	Management of Abdominal Distress
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